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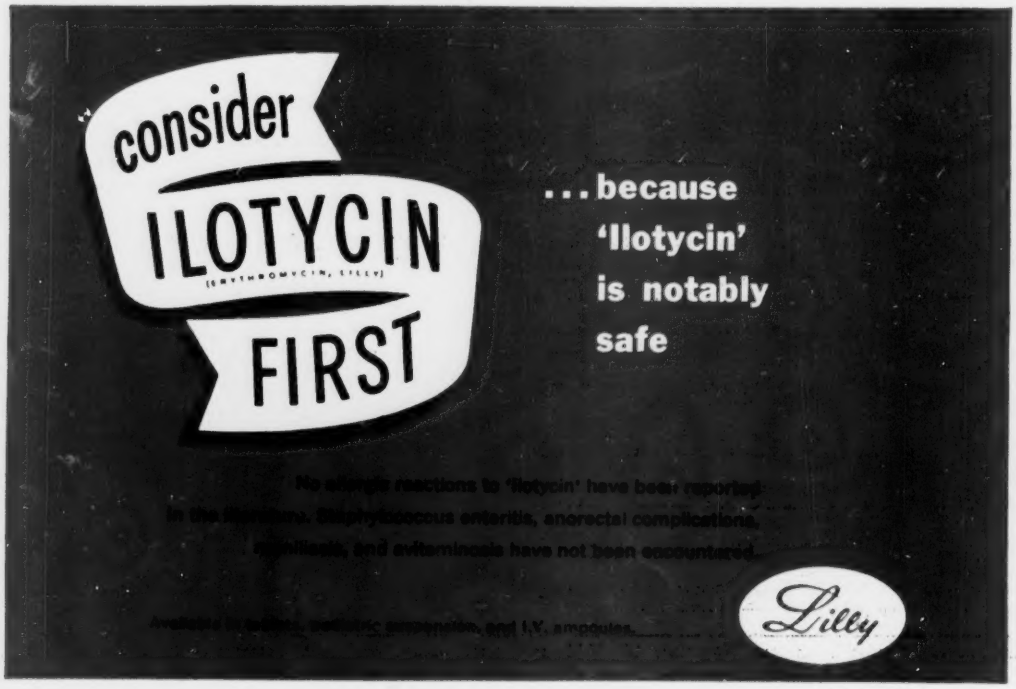

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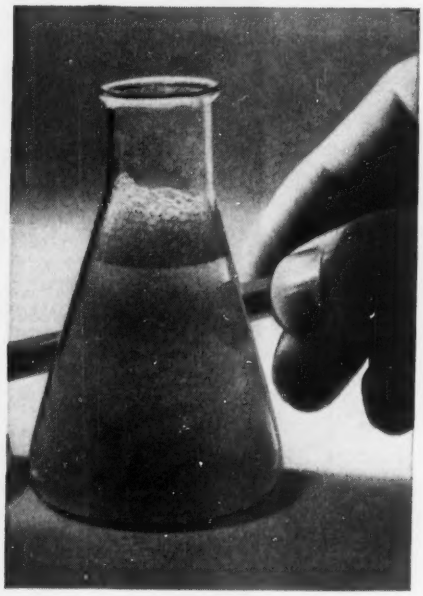

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1. *American Medical Association: New and Nonofficial Remedies, 1954. J. B. Lippincott Co., Philadelphia, p. 147*
2. *Scott, R. L., and others: Antibiot. & Chemo. 4:691 (June) 1954*

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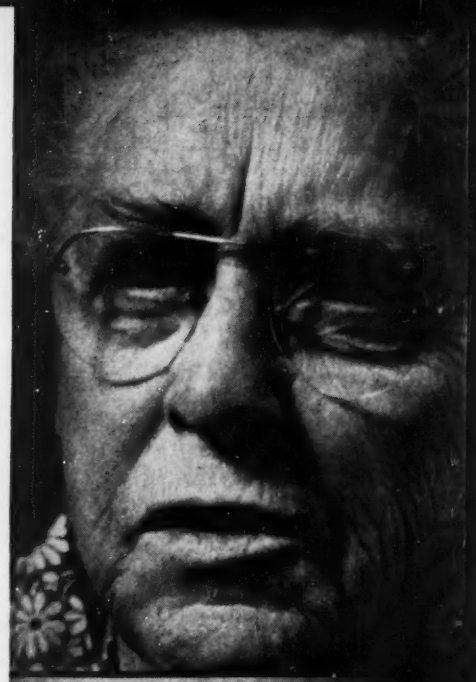

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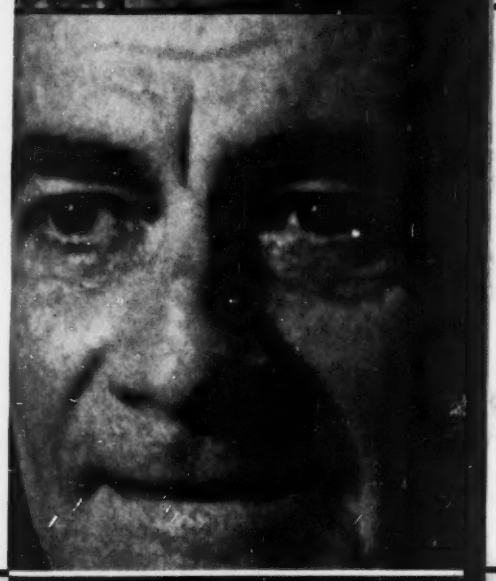

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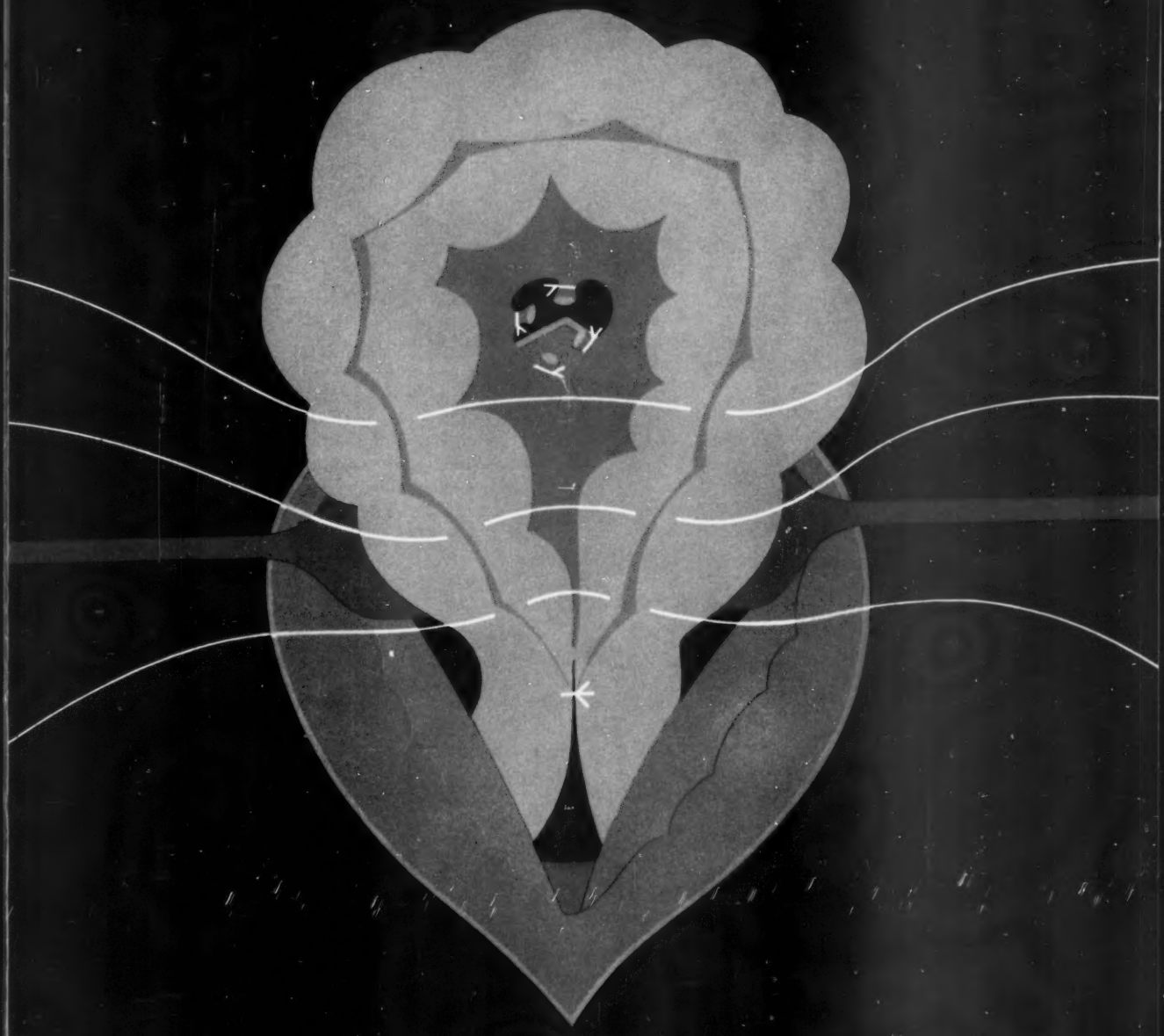

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1. Goldsmith, G. A.: Application to Human Nutrition, in Bourne, G. H., and Kidder, G. W.: Biochemistry and Physiology of Nutrition, New York, Academic Press Inc., 1953, chap. 23, p. 505.
2. Recommended Dietary Allowances, Washington, D. C., National Academy of Sciences—National Research Council, Publication 302, 1953, p. 23.
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4. Sherman, H. C.: Chemistry of Food and Nutrition, ed. 8, New York, The Macmillan Company, 1952, (a) p. 30; (b) p. 198; (c) p. 115; (d) p. 103.
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6. Smith, F. H.: The Use of High Fat Diets for Constipation, J.A.M.A. *88*:628 (Feb. 26) 1927.
7. Okey, R.: Cholesterol Content of Foods, J. Am. Dietet. A. *21*:341 (June) 1945.

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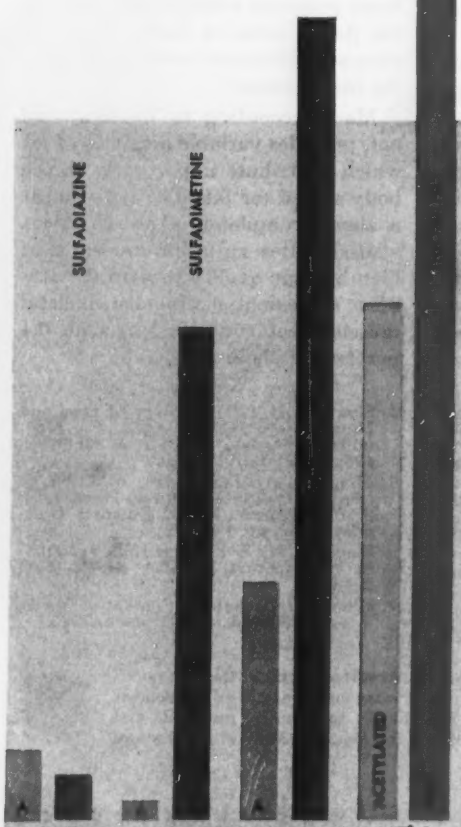

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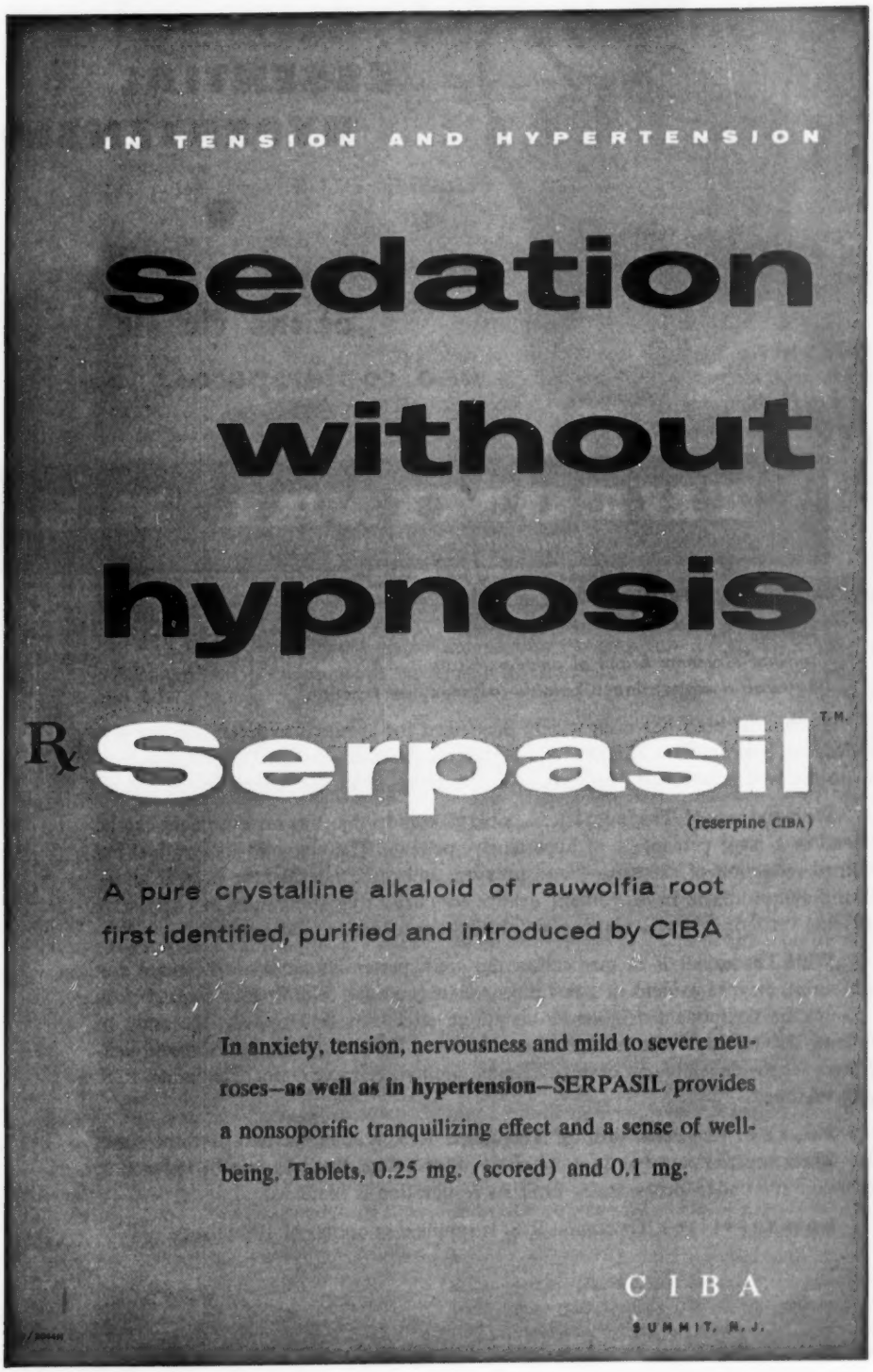
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EFFECT OF ANTIBIOTIC THERAPY ON MUCOVISCIDOSIS*

A Bacteriologic Study

MARIE R. H. STOPPELMAN, M.D.,† AND HARRY SHWACHMAN, M.D.‡

BOSTON

THERE are several reports in the literature concerning the influence of the various antibiotics on the bacterial flora of the nasopharynx and intestine.[1-4] In general, it has been observed that resistance may develop during therapy, or that the normal antibiotic-sensitive flora may be replaced by micro-organisms that are resistant to the agents used.[5-16] Particular attention has been given to the increased frequency of yeast and other fungi isolated during or after antibiotic therapy.[17-26] The effect of prolonged treatment with small daily doses of chlortetracycline and oxytetracycline on the bacterial flora in children with mucoviscidosis has been reported from this clinic.[27-30] No essential changes were noted in the flora of the throat and nasopharynx, and in most cases no effect was observed on the ærobic flora of the stools, whereas in some children a decrease in the normal flora was accompanied by the appearance and persistence of *Proteus vulgaris* and *Pseudomonas aeruginosa*.

The symptoms of mucoviscidosis, a disease often detected in infancy, are typically those resulting from pulmonary obstruction with mucus and the supervening or secondary lung infection, combined with the inspissation of the pancreatic secretion with failure of pancreatic enzyme production. The chief pulmonary features are chronic, often paroxysmal cough, chronic bronchitis, recurrent bronchopneumonia, bronchiectasis, chest deformity and digital clubbing. The roentgenograms of the chest may show areas of atelectasis and emphysema long before any detectable findings on physical examination. The main symptoms of pancreatic dysfunction are frequent and bulky foul stools, voracious appetite, failure to gain weight and a protuberant abdomen. The condition should not be confused with celiac disease, although in rare cases the differential diagnosis may be difficult.[31] The prognosis in untreated patients is poor, the majority succumbing to the extensive pulmonary infection in infancy or early childhood. A small number of untreated patients may survive childhood, indicating that the degree and severity of the pulmonary infection and the rate of progression of the pulmonary lesion are variable. The prognosis in patients treated with chlortetracycline and oxytetracycline has improved considerably, mainly because the pulmonary infections have been prevented or controlled. The striking clinical improvement and the details of management have been reported with chlortetracycline[28,32] and oxytetracycline,[30] both drugs showing a similar beneficial effect in the majority of patients treated. Continuous and prolonged antibiotic therapy has recently been evaluated[33] and will be the subject of a separate report.

The present report is concerned with the bacteriologic findings in 140 patients with mucoviscidosis, most of whom were treated with antibiotics for periods varying from a few months to five years. The age range of patients included in the present study was six months to fourteen years. Diagnoses were made and treatment given at the Children's Medical Center. The plan of treatment was as follows: patients with mild pulmonary involvement usually received chlortetracycline or oxytetracycline as the sole antibiotic at a dosage level of between 5 and 25 mg. per kilogram of body weight per day; in most cases the dosage was less than 20 mg. Forty per cent of all the patients who were treated with either chlortetracycline or oxytetracycline had also received, at the time the cultures were taken, either an additional antibiotic or a sulfonamide. The drug was given daily and continuously with few exceptions. Patients with moderate to extensive pulmonary involvement usually received a combination of agents, such as sulfadiazine, chloramphenicol, or erythromycin, in addition to chlortetracycline or oxytetracycline. Those with extensive lesions were usually given penicillin and streptomycin aerosol therapy in short courses for two or three weeks and rarely for longer periods. Dietary therapy consisted of a high-protein, high-

*From the Division of Clinical Laboratories and the Department of Medicine, Children's Medical Center, and the Department of Pediatrics, Harvard Medical School.

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†Fellow in medicine, Department of Pediatrics, Harvard Medical School and Children's Medical Center; fellow, American Association of University Women on leave of absence from the Children's Hospital of the University of Amsterdam (aided by Travel Grant from Fulbright Foundation).

‡Assistant professor of pediatrics, Harvard Medical School; chief, Division of Clinical Laboratories, Children's Medical Center.

calorie, slightly reduced fat intake in addition to water-miscible multivitamins. Pancreatin-replacement therapy was used in almost every case.

Nasopharyngeal Flora

The nasopharyngeal swab was taken by the oral rather than by the nasal route, to avoid contamination by the nasal bacterial flora as well as contamination from the mouth or tongue. This technic was not employed in previous studies. It was believed that a culture from a nasopharyngeal swab taken by the oral route would be more representative of the micro-organisms involved in pulmonary inflammations, since Auger[34] and Alexander et al.[35] had shown that in children with inflammation of the lower respiratory tract the etiologic micro-organisms could be found in the nasopharyngeal mucus either in pure culture or in predominant numbers.

Table 1. *Predominance of Pyogenic* Staph. aureus *in the Nasopharynx in Relation to Treatment.*

Therapy	Total No. of Cases	Cases with Predominance of Staphylococci	
		No.	Percentage
Chlortetracycline	66	6	9.1
Oxytetracycline	53	15	28.4
Chlortetracycline combined with other antibiotic or sulfonamide	38	21	55.2
Oxytetracycline combined with other antibiotic or sulfonamide	28	11	39.3
None	15	8	—

A total of 200 swabs from 140 patients were studied. One culture was taken in 95 patients, 2 cultures in 30 patients and 3 cultures in 15 patients. Fifty per cent of patients with mild, 53.8 per cent of those with moderate, and 65.0 per cent of those with severe disease had 1 culture. Those who had 2 and 3 cultures were equally distributed so far as the degree of pulmonary involvement was concerned. The interval between swabs in cases examined more than once was as follows: one month in 6 cases, two months in 15 cases, three months in 15 cases, four months in 10 cases, five months in 6 cases and six months in 8 cases. The period under treatment at the time of the examination of the nasopharyngeal mucus varied from one month to six years as follows: one month, 6 cases; two months to six months, 28 cases; six months to a year, 25 cases; over a year, 126 cases.

Table 2. *Predominance of* Staph. aureus *in the Nasopharynx in Relation to Pulmonary Involvement.*

Pulmonary Involvement	Total No. of Cases	Cases with Predominance of Staphylococci	
		No.	Percentage
Mild	88	7	7.8
Moderate	39	15	38.4
Far advanced	46	31	67.4

Prevalence of *Staphylococcus aureus*

The pyogenic staphylococci were differentiated by the production of hemolysis on 5 per cent horse-blood agar and their ability to grow in Evans's synthetic medium, which does not contain biotin.[36] Hemolysis and ability to grow in this synthetic medium coincided in 219 strains of staphylococci. Ten hemolytic strains and all 58 nonhemolytic strains isolated did not grow in this medium. The patients were divided according to the antibiotics employed, with a further subdivision on the basis of the results of nasopharyngeal cultures — that is, cultures in which staphylococci represented more than half the total flora isolated on 5 per cent horse-blood agar and those in which staphylococci were not predominant. The number of cases in which pyogenic staphylococci were predominant in the nasopharyngeal mucus was much less among patients treated with chlortetracycline than among those treated with oxytetracycline (Table 1). These two groups were directly comparable in degree of pulmonary involvement. These were the patients who could be kept in fairly good condition with only one of the antibiotics. The predominance of staphylococci was much higher in the nasopharyngeal mucus from patients treated with combined antibiotics than in those treated with either chlortetracycline or oxytetracycline alone.

Table 3. *Prevalence of* P. vulgaris, Ps. aeruginosa *and Yeastlike Fungi in the Nasopharynx.*

Treatment	Total No. of Cases	Cases with Yeasts		Cases with Either Pseudomonas or Proteus	
		No.	Percentage	No.	Percentage
Chlortetracycline	66	4	6	11	16.6
Chlortetracycline & other antibiotic or sulfonamide	38	4	10.5	10	26.3
Oxytetracycline	53	6	11.3	24	45.2
Oxytetracycline & other antibiotic or sulfonamide	28	3	10.7	9	32.1
None	15	0	—	0	—

Pyogenic staphylococci were predominant in the nasopharyngeal mucus of 7.8 per cent of the patients with mild involvement of the respiratory tract as compared to 38.4 per cent in the group of children with moderate pulmonary involvement (Table 2). The occurrence of *Staph. aureus* in predominant numbers in the nasopharyngeal mucus increased to 67.4 per cent among those with far-advanced lesions in the lungs.

Prevalence of Yeastlike Fungi

The frequency of yeastlike fungi in the nasopharyngeal mucus of the different groups was variable (Table 3). None were isolated from untreated patients. However, this difference was of little signifi-

cance, since the group of patients not under antibiotic therapy was too small to warrant statistical analysis.

Prevalence of *P. vulgaris* and *Ps. aeruginosa*

P. vulgaris and *Ps. aeruginosa* were isolated in 16.6 per cent of the patients treated with chlortetracycline and in 45.2 per cent of those receiving oxytetracycline. Similar significant differences were observed between those treated with chlortetracycline alone or in combination with other antibiotics or sulfonamides and those given oxytetracycline alone or in combination with other drugs (Table 3). *P. vulgaris* and *Ps. aeruginosa* were not isolated from a group of 15 patients who at the time of examination had not been treated with antibiotics. However, this group was too small to be of statistical significance.

Sensitivity tests were done by the usual tube-dilution method, tryptic digest broth being used.

A high percentage of strains of *Staph. aureus* isolated from children treated with chlortetracycline or oxytetracycline were resistant to these antibiotics, whereas only 2 of 11 strains isolated from untreated patients were resistant to either drug (Table 4). There appeared to be little difference in resistance between oxytetracycline and chlortetracycline, as had been reported previously.[38-40] Most of the resistant strains were still sensitive to relatively low concentrations of chloramphenicol. Twenty-three per cent of the staphylococci isolated were resistant to 10 units of penicillin per cubic centimeter. The 11 strains of staphylococci isolated from the children who had not received antibiotics were all sensitive to streptomycin, and a third of the strains isolated from patients under antibiotic therapy were resistant to 10 gamma of streptomycin per cubic centimeter.

TABLE 4. *Resistance of* Staph. aureus *from Nasopharynx to Antibiotics.*

TREATMENT	TOTAL NO. OF STRAINS	STRAINS RESISTANT TO 10 UNITS OF PENICILLIN	STRAINS RESISTANT TO 10 GAMMA OF STREPTOMYCIN	STRAINS RESISTANT TO 5 GAMMA OF CHLORTETRACYCLINE	STRAINS RESISTANT TO 5 GAMMA OF OXYTETRACYCLINE	STRAINS RESISTANT TO 5 GAMMA OF CHLORAMPHENICOL
		%	%	%	%	%
Oxytetracycline alone or combined with other antibiotic or sulfonamide	33	24.2	33.3	84.4	94.0	6.1
Chlortetracycline alone or combined with other antibiotic or sulfonamide	39	23.0	35.9	89.7	89.7	15.4
None	11	(2 cases)	—	(2 cases)	(2 cases)	—

An evaluation was made of the percentage of the bacteria in each aerobic culture that showed resistance to the various antibiotics (Table 5). The mean percentage of resistant bacteria in each group then was computed from these percentages. Thirty to forty per cent of the aerobic flora were resistant to penicillin, streptomycin and chloramphenicol.

TABLE 5. *Sensitivity of Nasopharyngeal Flora.*

TREATMENT	NO. OF SWABS	MEAN PERCENTAGE RESISTANT TO 10 UNITS OF PENICILLIN	MEAN PERCENTAGE RESISTANT TO 10 GAMMA OF STREPTOMYCIN	MEAN PERCENTAGE RESISTANT TO 5 GAMMA OF CHLORTETRACYCLINE	MEAN PERCENTAGE RESISTANT TO 5 GAMMA OF OXYTETRACYCLINE	MEAN PERCENTAGE RESISTANT TO 5 GAMMA OF CHLORAMPHENICOL
Oxytetracycline alone or combined with other antibiotic or sulfonamide	41	32.7	30.5	85.3	91.3	36.9
Chlortetracycline alone or combined with other antibiotic or sulfonamide	43	36.4	32.6	91.0	88.0	43.4
None	15	2.0	4.4	9.9	26.0	5.4

Antibiotic Sensitivity of Nasopharyngeal Flora

All micro-organisms isolated from the aerobic cultures of the nasopharynx of 100 patients were tested for sensitivity with the various antibiotics. Strains that were resistant to 10 units of penicillin or 10 gamma of streptomycin per cubic centimeter were considered to be resistant, whereas levels of 5 gamma of chlortetracycline, oxytetracycline and chloramphenicol were chosen to indicate resistance. The selection of these in vitro levels was arbitrary, since it is well known that for various reasons in vitro and in vivo response to an antibiotic are not necessarily parallel.[37]

Erythromycin. Nine children received erythromycin,[41-45] usually in combination with chlortetracycline (Cases 1, 2, 4, 5, 6 and 7). Three patients (Cases 2, 3 and 4) received penicillin and streptomycin aerosol in addition. One patient (Case 3) received

chloramphenicol, and another (Case 8) Gantrisin. Only 1 child (Case 9) was treated with erythromycin alone. Resistance to erythromycin developed in 3 strains of *Staph. aureus* (Table 6).

Bacterial Flora of Stools

Rectal swabs were obtained from 150 patients with mucoviscidosis, who received antibiotics, and from 152 children, who came to the Out-Patient Department for other causes and were not treated with antibiotics. Swabs were cultured on 5 per cent horse-blood agar, eosin methylene blue agar, Chapman–Stone agar[46,47] and Sabouraud's agar.

Table 6. *Effect of Erythromycin Treatment.*

Case No.	Sensitivity of *Staph. aureus* Before Therapy	Duration of Treatment	Sensitivity after Treatment
	gamma/cc.	*mo.*	*gamma/cc.*
1	0.25	1	0.25
		3	0.25
		4	0.25
2	0.25	4	10.0
3	0.25	2½	0.25
4	0.125	1	1.25
		4	2.5
5		2	0.125
		4	0.125
6	0.125	2	0.25
		4	0.25
7		4	0.25
8	0.125	2	0.125
		3	10.0
9		2	10.0

Pyogenic staphylococci were isolated from 179 of 302 rectal swabs. Both the blood-agar plate and the Chapman–Stone medium were positive with pyogenic staphylococci in 118 cases, whereas in 55 cases positive cultures were obtained on the Chapman–Stone medium only. There were 6 cases in which the blood-agar plate alone was positive. A comparison of the aerobic flora of the stool as assayed by examination of rectal swabs is summarized in Table 7. *Staph. aureus, P. vulgaris* and yeastlike fungi were isolated more frequently from the stools of patients with mucoviscidosis receiving antibiotics than from those of children in the control group, whereas the prevalence of streptococci was lower than that in the control group. No significant difference was found in the frequency of *Escherichia coli* in either group.

Table 7. *Comparison of Stool Flora in Patients Receiving Antibiotics with Those of Control Children.*

Group	Total No. of Rectal Swabs	*P. vulgaris*		Streptococcus		*Staph. aureus*		Yeastlike Fungi	
		No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage
Patients treated with antibiotics	150	79	52.6	20	14.8	100	66	28	18.5
Control	152	15	9.8	54	35.5	79	52	12	7.9

Discussion

The predominance rather than the frequency of pyogenic staphylococci was compared, since the former may eventually provide a better indication of the micro-organism involved in the inflammatory process of the lower respiratory tract. The predominance of staphylococci in patients treated with antibiotics ranged from 9 to 55 per cent whereas the frequency was higher, ranging from 39 to 74 per cent. This difference may be important since previous experience has shown that in the absence of antibiotic therapy the etiologic agent of pulmonary inflammation in these cases invariably was *Staph. aureus.*[48]

Comparison of the groups treated with chlortetracycline and oxytetracycline shows that the percentage of predominance of staphylococci is lower in the chlortetracycline treated group. The 2 groups, as mentioned previously, were comparable clinically and received the same schedule of dosage. In general these were the milder cases, and their clinical response to therapy was considered satisfactory. The patients with far-advanced pulmonary changes showed a higher percentage of predominance of staphylococci.

The prevalence of yeastlike fungi was low, varying from 6 to 11.3 per cent. This low figure, as compared with the findings of other studies, in which throat swabs were cultured, may have been due to the fact that fungi are more likely to grow on the mucous membranes of the mouth, tongue and throat than in the nasopharynx. Pseudomonas and proteus were isolated more frequently in the children treated with oxytetracycline alone or in combination with other drugs than in the children who received chlortetracycline alone or combined with other antibiotics or sulfonamide.

Consideration of the differences in the predominance of pyogenic *Staph. aureus* and in the frequency of pseudomonas and proteus in the patients treated with chlortetracycline and oxytetracycline suggests that chlortetracycline is preferable from a bacteriologic point of view. However, a difference in clinical response in spite of those apparent differences in bacteriologic response between the two antibiotics has not been noted. Eighty-five to 94 per cent of the strains of staphylococci isolated from the nasopharyngeal swabs of patients treated with chlortetracycline or oxytetracycline alone or in combination with other antibiotics or sulfonamides were resistant to these antibiotics. Eighty-five to 91 per cent of the aerobic

flora of the nasopharynx was resistant to chlortetracycline and oxytetracycline in these groups. Most of the staphylococci isolated were still sensitive to chloramphenicol probably owing to lack of previous exposure to this agent. The low frequency of penicillin-resistant strains of staphylococci in these patients may also have been due to the relatively infrequent use of penicillin since the introduction of chlortetracycline. In a previous study (1949) 19 of 26 strains of staphylococci isolated from the nasopharynx were resistant to 4 units of penicillin, whereas in this study only 22 of 72 strains were found to be resistant to 5 units of penicillin. No difference in the occurrence of resistance was noted between the group of children treated continuously with chlortetracycline or oxytetracycline for less than six months and the group of children who had been treated for a longer period. A satisfactory clinical response could be obtained with either antibiotic in spite of the presence of resistant micro-organisms in the nasopharynx of these patients. Determination of the sensitivity of the micro-organisms isolated from the nasopharynx did not provide a guide to the selection of the antibiotic of choice.

It is not clear why chlortetracycline or oxytetracycline continued to have beneficial therapeutic effects despite the in vitro resistance of the micro-organisms isolated from the nasopharynx. In patients with minimal pulmonary involvement treated with chlortetracycline the beneficial clinical response frequently correlated with the disappearance of the *Staph. aureus* from the nasopharynx. This suggests that the antibiotic acts as more than a prophylactic agent in preventing the acquisition of new infections.

A number of questions have arisen in the management of patients with mucoviscidosis, such as continuous versus intermittent antibiotic therapy, rotation of agents and the use of various combinations. This aspect of the problem is considered elsewhere.[33]

Summary

The aerobic flora of the nasopharynx and stools were studied in 140 patients with mucoviscidosis, who had received antibiotic therapy continuously for periods of as long as six years. The relation of such prolonged therapy to changes in bacterial flora and the occurrence of antibiotic resistance is discussed.

These observations confirm the previous conclusion that, despite the appearance of antibiotic resistance in the nasopharyngeal flora of these patients, satisfactory clinical response may still be obtained.

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CHANGES IN PRESSURES IN THE LEFT ATRIUM AND PULMONARY ARTERY IMMEDIATELY BEFORE AND AFTER MITRAL VALVULOPLASTY*

PAUL N. YU, M.D.,† FRANK W. LOVEJOY, JR., M.D.,† ROBERT E. NYE, JR., M.D.,‡ HOWARD A. JOOS, M.D.,§ DAVID C. BEATTY, M.D., M.R.C.P.,¶ AND EARLE B. MAHONEY, M.D.‖

ROCHESTER, NEW YORK

SIMULTANEOUS recording of pressures in the left atrium and pulmonary artery in patients with mitral stenosis at operation was first described by Munnel and Lam,[1] who showed that successful mitral commissurotomy usually caused a marked decrease in the atrial and some decline in the pulmonary-artery pressure. Pressure changes in the left atrium before and after mitral valvulotomy have also been reported by Wynn and his associates.[2] These authors described various pressure patterns in mitral stenosis before operation, and noted little change in the form of the pressure pulse after operation. Connolly and his co-workers,[3] recording simultaneous pressure in the left atrium and pulmonary-artery wedge pressure in 12 patients with mitral stenosis, found the pattern and the magnitude of the two pressures almost identical in a given patient; an immediate decrease of approximately equal magnitude in both pressures followed satisfactory mitral commissurotomy.

Parker et al.[4] reported immediate changes in the respective pressures in 21 patients during mitral commissurotomy — usually an immediate drop. The percentage reduction was higher for the pressure in the left atrium than for that in the pulmonary artery. Reduction of pressures in patients with excellent results was greater than that in those with or without improvement.

It is the purpose of this study to describe the pressure patterns in the left atrium and pulmonary artery in 25 patients with mitral stenosis, and to correlate the immediate change in these pressures with the clinical response after mitral valvuloplasty.

METHOD AND MATERIAL

Under general ether and oxygen anesthesia the left atrial appendage and atrium were exposed by a left lateral thoracotomy. Pressure tracings in the left atrium and pulmonary-artery trunk were recorded through a 22-gauge needle attached to a Hathaway pressure manometer and a Sanborn poly-viso cardiette. Pressures were recorded before and immediately after fracture of the mitral valve and removal of the atrial appendage. In each case the preoperative and postoperative punctures in the left atrium and pulmonary artery were made as close together as possible. The gauge and needle were flushed and refilled with sodium citrate solution after each recording. The gauge was calibrated with a mercury manometer. An electrocardiogram (Lead 2) was recorded simultaneously.

Twenty-five patients with predominant mitral stenosis who underwent mitral valvuloplasty were included. Twenty-two were closely followed for periods of three months to two years after operation, and 3 patients died within three days of operation.

The clinical response was graded as follows: "excellent result," signifying attainment of Class I of the functional classification of the New York Heart Association[5]; "significant improvement," signifying reclassification from Class IV to III or from Class III to II; and "no improvement." In the last group 1 patient remained in Class IV, and 2 in Class III.

The pressures before and after mitral valvuloplasty in 25 patients with mitral stenosis are presented in Table 1 and plotted in Figures 1 and 2.

RESULTS

Pressure in Left Atrium

Pressure patterns in patients with sinus rhythm. Pressure patterns from the left atrium in patients with mitral stenosis and sinus rhythm resemble those of normal subjects as described by Wynn and his associates[2] (Fig. 3). There are usually two peaks, one preceding the QRS complex of the electrocardiogram from atrial systole and another following the T wave and corresponding to late ventricular systole. The second peak falls rapidly with opening of the mitral valve. This pattern is similar to that of the pulmonary-artery wedge pressure recorded by Connolly et al.[3] In some cases the first peak may be slightly taller than the second; in others the reverse may occur.

Pressure patterns in patients with atrial fibrillation. In patients with mitral stenosis and atrial fibrillation the pressure tracing shows a distinct rise at the onset of ventricular systole and reaches its peak or remains at a plateau in late systole. There may be a small notch immediately after the QRS complex, but the peak due to atrial systole before QRS seen in patients

*From the departments of Medicine, Surgery and Pediatrics, University of Rochester School of Medicine and Dentistry, and the Medical and Surgical Clinics, Strong Memorial and Rochester Municipal hospitals.

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†Assistant professor of medicine, University of Rochester School of Medicine and Dentistry; assistant physician, Strong Memorial and Rochester Municipal hospitals.

‡Postgraduate fellow in medicine, University of Rochester School of Medicine and Dentistry.

§Assistant professor of pediatrics, University of Rochester School of Medicine and Dentistry; assistant pediatrician, Strong Memorial and Rochester Municipal hospitals.

¶Ebsary Fellow in Medicine, University of Rochester School of Medicine and Dentistry.

‖Associate professor of surgery, University of Rochester School of Medicine and Dentistry; associate surgeon, Strong Memorial and Rochester Municipal hospitals.

with sinus rhythm is absent. The pressure rise tends to be greater with faster ventricular rates and after a shorter preceding diastole, as described by Wynn and his co-workers.[2]

Magnitude immediately before mitral valvuloplasty. In normal subjects mean left atrial pressure does not exceed 10 mm. of mercury. Of our patients only 4 had pressures less than 20 mm., and 2 had pressures above 40 mm. of mercury. The average value before valvuloplasty was 28 mm. The magnitude of pressure before fracture of the valve had no bearing on the clinical response to operation (Table 1).

TABLE 1. *Pressures in the Left Atrium and Pulmonary Artery before and after Mitral Valvuloplasty.*

PATIENT	PREOPERATIVE FUNCTIONAL CLASSIFICATION	MEAN PRESSURE IN LEFT ATRIUM				MEAN PRESSURE IN PULMONARY ARTERY			
		BEFORE OPERATION	AFTER OPERATION	DECREASE	DECREASE	BEFORE OPERATION	AFTER OPERATION	DECREASE	DECREASE
		mm. Hg.	*mm. Hg.*	*mm. Hg.*	%	*mm. Hg.*	*mm. Hg.*	*mm. Hg.*	%
Group I*:									
N.P.	III	42	14	28	67	75	52	23	31
C.A.	III	39	18	21	54	44	37	7	16
E.A.	III	38	25	13	34	54	48	6	11
F.L.	III	31	13	18	58	44	31	13	30
M.N.	III	27	13	14	52	53	38	15	28
G.W.	II	25	17	8	32	33	25	8	24
P.V.	III	21	17	4	19	66	63	3	5
H.M.	II	19	13	6	32	29	27	2	7
V.J.	III	17	10	7	41	31	31	0	0
D.P.	III	17	9	8	47	—	27	—	—
Averages		28	15	13	44	48	38	9	17
Group II†:									
J.R.	III	35	25	10	29	39	36	3	8
C.S.	III	34	23	11	32	68	58	10	15
J.B.	III	28	19	9	32	64	35	29	45
L.F.	III	27	25	2	7	47	33	14	30
M.S.	III	25	22	3	12	58	49	9	16
P.P.	III	23	13	10	43	35	22	13	37
E.C.	IV	22	18	4	18	50	49	1	2
C.C.	III	20	12	8	40	53	29	24	45
E.R.	III	16	15	1	6	33	37	−4	−12
Averages		25	19	6	24	50	39	11	21
Group III‡:									
J.C.	IV	35	31	4	11	47	45	2	4
E.K.	III	32	27	5	16	77	57	20	26
P.D.	III	24	25	−1	−4	40	—	—	—
Averages		30	28	2	8	55	51	11	15
Group IV§:									
B.R.	III	42	17	25	60	80	69	11	14
A.C.	IV	39	28	11	28	—	—	—	—
L.R.	IV	20	11	9	45	42	20	22	52
Averages		34	19	15	44	61	44	17	33

*Excellent result—patients attained functional Class I postoperatively.
†Significant improvement—patients reclassified from functional Class IV to III or from III to II after operation.
‡No improvement.
§Death within 3 days of operation.

Changes immediately after mitral valvuloplasty. The mean pressure declined by 4 mm. of mercury or more in all but 4 cases immediately after fracture of the valve. The largest decline was 28 mm. (from 42 to 14 mm.). The average decline for all patients was 10 mm., or 32 per cent of the preoperative values. In 9 patients the mean pressure fell to 14 mm. or less, the lowest postoperative pressure being 9 mm. of mercury.

Comparison between clinical response and immediate postoperative decrease in mean pressure revealed good correlation. In general, the patients who improved most were those in whom the reduction was greatest. When no clinical improvement occurred the decrease was small. In Group I, with excellent results, the pressure fell more than 12 mm. of mercury in half the patients. The drop was less than 30 per cent of the preoperative pressure in only 1 patient. The average reduction for this group was 13 mm., or 44 per cent of the preoperative pressure. In Group II, with significant improvement, no patient achieved a decrease of 12 mm. of mercury and in 5 of the 9 cases the fall was less than 30 per cent of the preoperative pressure. In Group III, with no improvement, the decline was meager. One of these patients had a negligible increase in pressure after valve fracture. Two of the 3 patients in Group IV who died within three days of operation were in functional Class IV, and the third was in Class III. They all achieved a distinct reduction in mean pressure. In patients A.C. and L.R. the cause of death was cerebral embolism. In patient B.R., whose mean pressure dropped from 42 to 17 mm. of mercury, autopsy revealed a highly successful mitral valvuloplasty. The cause of death was massive pulmonary embolism on the third postoperative day.

In no case did significant mitral insufficiency follow mitral-valve surgery. This was supported by the absence of a regurgitant jet on palpation and by the failure of pressure in the left atrium to rise significantly during ventricular ejection. However, a Grade 2 apical systolic murmur was heard a few days after operation in 5 cases.

Comparison with pulmonary "capillary" pressure. Pressure in the left atrium measured before fracture at operation was compared with pulmonary "capillary" pressure (pulmonary-artery wedge pressure) obtained during previous cardiac catheterization in 18 patients, and measurements after fracture at operation with wedge pressures obtained during subsequent cardiac catheterization in 8 patients (Table 2). Although the conditions under which the pressures were measured are not comparable, the two mean pressures agreed within 3 mm. of mercury in more than half the cases. However, in several cases a considerable discrepancy existed. Similarity in the two pressure patterns was identified in only a few cases.

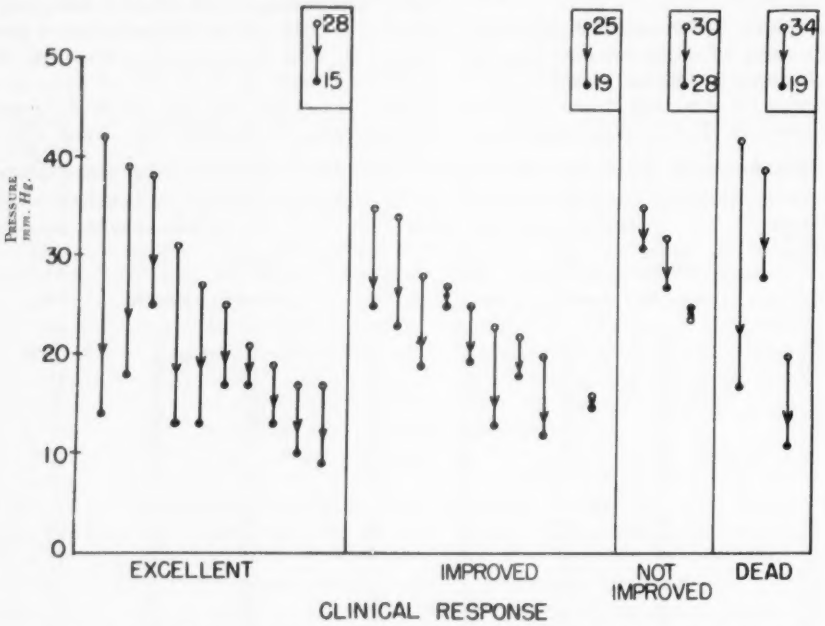

FIGURE 1. *Pressure in the Left Atrium Immediately before and after Mitral Valvuloplasty in 25 Patients.*

The preoperative and postoperative values are represented respectively by hollow and solid circles. The figures in the blocks on the right-hand side indicate the average mean pressures before and after operation in each group.

Pulmonary-Artery Pressure

Pressure patterns. The pattern in patients with mitral stenosis obtained directly at operation was similar to that obtained during cardiac catheterization (Fig. 3). The systolic rise in pressure occurred just after the R wave of the electrocardiogram. The peak was usually rounded and was followed by a gradual fall. In most cases a dicrotic notch occurred in the upper descending limb, indicating closure of the pulmonic valve. After the dicrotic notch the pressure declined to the diastolic level, usually coinciding with the beginning or peak of the succeeding R wave in the electrocardiogram.

In patients with sinus rhythm the systolic and diastolic pressures varied slightly in successive beats, but in patients with atrial fibrillation moderate or marked variation of pressure from beat to beat was frequent. The pulmonary-artery diastolic pressure usually approximated the mean pressure in the left atrium although in several cases the former was much higher.

Magnitude immediately before mitral valvuloplasty. In normal subjects mean pulmonary-artery pressure does not exceed 20 mm. of mercury. In our patients the pressures ranged from 29 to 80, with an average of 52 mm. The magnitude before valve fracture appeared unrelated to the clinical response to operation.

Changes immediately after mitral valvuloplasty. Satisfactory measurements of pulmonary-artery pressure before and after fracture were obtained in 22 patients. In 15 of these, the pressure declined by 5 mm. of mercury or more. The maximum decrease was 29 mm., and the average reduction for all patients was 10 mm. of mercury, or 20 per cent. In general the diastolic pressure declined more than the systolic pressure.

Comparison between clinical response and immediate postoperative decrease in the mean pulmonary-artery pressure revealed no correlation whatever. This was true whether the decline was expressed in absolute terms or as a percentage of the initial pressure.

Discussion

At present the only safe method of recording pressure in the left atrium is under direct vision at tho-

racotomy; repeated punctures may be made with relative safety. The transthoracic method[6,7] is not without danger, and its general use awaits further trial and improvement in technic.

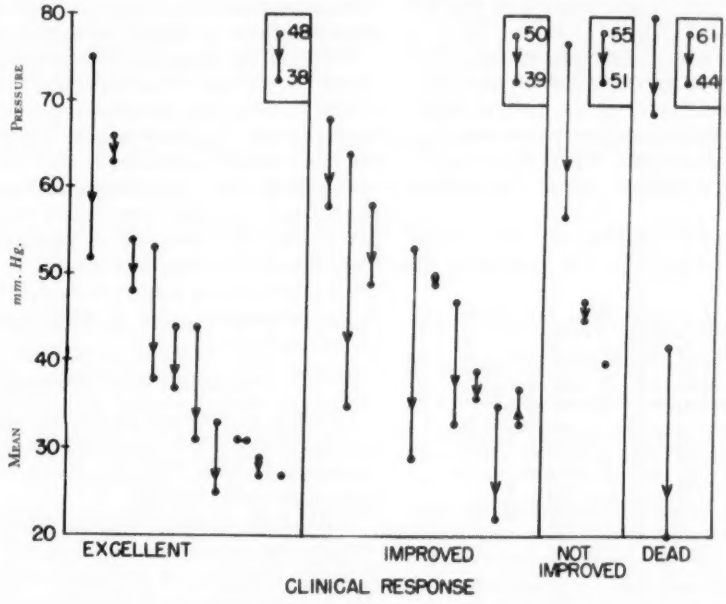

FIGURE 2. *Pulmonary-Artery Pressure Immediately before and after Mitral Valvuloplasty in 22 Patients.*

The preoperative and postoperative values are represented respectively by hollow and solid circles. The figures in the blocks on the right-hand side indicate the average mean pressures before and after operation in each group.

mated by palpation of the mitral-valve orifice during operation or, less reliably, by calculation of mitral-valve area by means of the hydraulic formula.[8] In general the more severe the obstruction, the higher the pressure in the left atrium, and the greater the functional disability. Since the recording of atrial pressure is not a routine practice in assessing the de-

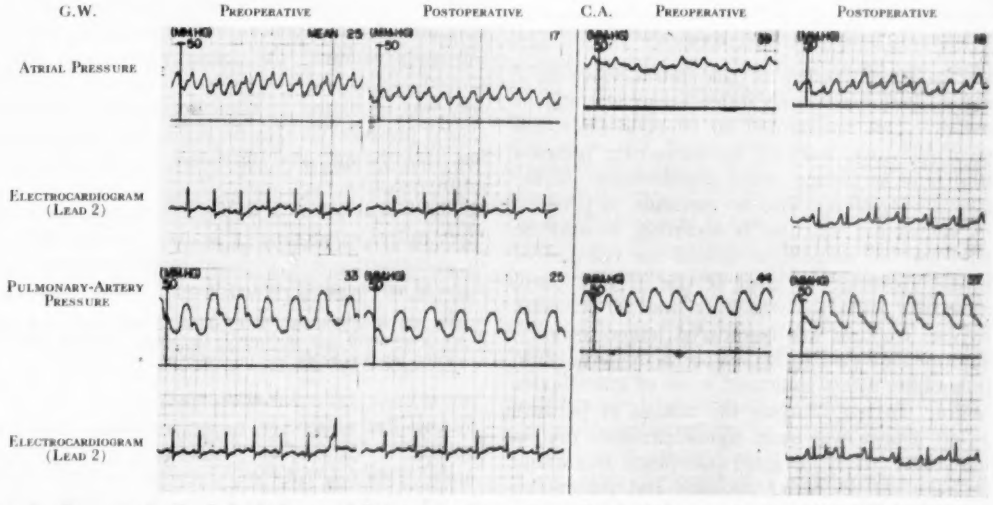

FIGURE 3. *Pressures in the Left Atrium and Pulmonary Artery Immediately before and after Mitral Valvuloplasty, with Simultaneous Electrocardiograms, in Patients G.W. and C.A.*

The values of the mean pressure are given on the right-hand side of each tracing. It is possible that the preoperative pulmonary-artery-pressure tracing in C.A. was damped.

Increased pressure in the left atrium almost always accompanies significant narrowing of the mitral valve. The degree of obstruction may be esti-

gree of mitral stenosis, the measurement of the pulmonary "capillary" pressure by cardiac catheterization may be a fair index of the pressure in the left atrium.[3,9,10]

Patients with significant mitral insufficiency may have an appreciable elevation in atrial pressure during ventricular ejection.[11] One of the cases of Munnel and Lam[1] demonstrated an increase during ventricular systole after unsuccessful mitral commissurotomy, indicating that significant mitral insufficiency had been produced.

Since significant mitral insufficiency may follow mitral valvuloplasty, we recorded the pressure in the left atrium after fracture of the mitral valve in 3 patients while the surgeon's index finger was still in the atrium. This represented an effort to assess the adequacy of valve fracture by measuring pressure reduction and to detect mitral insufficiency. If the decrease is insignificant and no elevation of pressure during ventricular ejection is recorded, it may be necessary for the surgeon to extend the fracture of the valve. However, in each of the 3 cases cited, the immediate reduction was more than 30 per cent, and further fracture was considered unnecessary.

TABLE 2. *Comparison of Pressure in the Left Atrium with Pulmonary "Capillary" Pressure.*

PATIENT	MEAN PRESSURE IN LEFT ATRIUM		MEAN PULMONARY "CAPILLARY" PRESSURE	
	BEFORE OPERATION	AFTER OPERATION	BEFORE OPERATION	AFTER OPERATION
	mm. Hg.	*mm. Hg.*	*mm. Hg.*	*mm. Hg.*
A.C.	39	28	39	—
C.A.	39	18	38	15
J.R.	35	25	33	—
J.B.	28	19	31	17
F.L.	31	13	30	—
G.W.	25	17	27	—
P.P.	23	13	26	—
P.D.	24	25	21	26
C.C.	20	10	20	—
L.F.	27	25	39	—
E.K.	32	27	36	—
B.R.	42	17	34	—
L.R.	20	11	34	—
E.C.	22	18	32	—
E.A.	38	25	29	20
J.C.	35	31	27	—
C.S.	34	23	25	—
V.J.	17	10	21	14
P.V.	21	17	—	15
N.P.	42	14	—	22
M.S.	25	22	—	23

The immediate decline in pressure in the left atrium and pulmonary artery indicated relief of mitral-valve obstruction. In our 25 cases the change of pressure in the left atrium was more significant than that in the pulmonary artery. A good correlation was found between the fall in atrial pressure and subsequent clinical response. This was supported by the measurement of pulmonary "capillary" pressure in 5 patients during cardiac catheterization several months later. In 3 patients with excellent results and in 1 with significant improvement pulmonary "capillary" pressure was greatly reduced as compared with preoperative values. In 1 patient with no improvement postoperative pulmonary "capillary" pressure was actually higher than the preoperative value. However, clinical improvement in certain cases may be striking despite little or no change on cardiac catheterization.

Although the mean pulmonary-artery pressure declined in all but 2 patients, no good correlation existed between the decrease and subsequent clinical improvement. Furthermore, in several patients the pressure recorded immediately after operation showed only a slight fall. Yet cardiac catheterization a few months later revealed a significant reduction as compared with the preoperative measurement. Therefore, it is our opinion that the fall in atrial pressure during mitral-valve surgery is more reliable than that in the pulmonary artery in indicating the adequacy of the operation.

SUMMARY AND CONCLUSION

Changes in pressures in the left atrium and pulmonary artery before and immediately after mitral valvuloplasty were studied at thoracotomy in 25 patients with mitral stenosis.

With sinus rhythm the atrial pressure pattern resembled the normal pattern, but with atrial fibrillation the peak due to left atrial systole was absent. Most patients showed a significant decline from elevated levels of atrial pressure immediately after valvuloplasty. Ultimate clinical response correlated with the pressure change at operation. Preoperative mean pressure in the left atrium approximated earlier measurement of pulmonary-artery wedge pressure in about half the cases.

The pattern of pulmonary-artery pressure resembled that observed during earlier cardiac catheterization, and the pulmonary-artery diastolic pressure usually approximated the mean pressure in the left atrium. Pulmonary hypertension occurred uniformly and was unrelated to clinical response. Pulmonary-artery pressure usually declined after valvuloplasty, but the change was unrelated to ultimate clinical improvement.

The fall in pressure in the left atrium immediately after mitral-valve surgery is more reliable than that in pulmonary-artery pressure in the prognosis of the clinical response of patients with mitral stenosis.

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PATHOGENESIS AND SURGICAL MANAGEMENT OF ACUTE GASTRIC EROSIONS*

Report of a Case

ERNEST L. SARASON, M.D.,† AND BENJAMIN F. LEVY, JR., M.D.‡

SYRACUSE, NEW YORK

WHEREAS a great deal of attention has been focused on the therapy of peptic ulcer and its complications, relatively little heed has been given to acute gastric erosions—a definite pathologic entity differing from acute peptic ulcers in being more shallow. By virtue of the fact that gastric erosions invade no deeper than the muscularis mucosae, their presence often escapes the attention of gastroscopist, radiologist and surgeon. Despite their superficial location, it must be granted that acute gastric erosions may be responsible for massive hemorrhage, and because of their elusiveness in diagnosis, they are particularly dangerous. In the event of uncontrollable and massive hemorrhage, one must be aware that a surgical emergency may exist. (It should be pointed out in passing that acute gastroduodenal erosions do not necessarily become chronic peptic ulcers.) Although many factors have been incriminated in the development of acute gastroduodenal ulceration, it may eventually be shown that ulcers can occur under quite dissimilar conditions. It is our purpose to report a case of massive hematemesis due to acute gastric erosions that developed shortly after the onset of a cerebrovascular accident.

The association of acute ulceration of the upper gastrointestinal tract with a variety of central-nervous-system diseases has been the subject of considerable medical speculation for many years. Nearly a century ago Rokitansky[1] described gastromalacia as a sequela of acute brain affections including tuberculous meningitis, tabes, trauma and tumor. In general it seemed that, whatever the pathologic process, the primary brain areas involved were in the region of the hypothalamus and basal ganglions. It remained for Cushing,[2] in 1932, to reawaken clinicians to the possible etiologic relation of brain damage to peptic ulcer. In this scholarly Balfour lecture Cushing postulated that the acute gastric erosions were due to vagal stimulation stemming from disease of the hypothalamus, with resultant hypersecretion and hypermotility of the stomach. It was Cushing's thesis that a very delicate homeostatic balance normally existed between the sympathetic and parasympathetic nervous systems, and that the hypothalamus was the vagal center. He believed that this was the modus operandi of acute peptic ulcers in cases observed in association with neoplastic, inflammatory or vascular involvement of the hypothalamus.

In the immediately ensuing years a number of clinical and experimental reports supported Cushing's thesis in general. Hoff and Sheehan[3] described experimental gastric erosions that followed hypothalamic lesions in monkeys. Although the majority of observers, including Cushing, have regarded lesions of the hypothalamus as responsible for the acute peptic ulcerative process, a few articles have pointed out that such lesions are not necessarily present. Masten and Bunts,[4] Opper and Zimmerman[5] and Strassman[6] have reported so-called neurogenic gastric erosions in which the cerebral lesions—neoplastic, vascular or inflammatory—*did not involve* the hypothalamus and midbrain region. Opper and Zimmerman postulated that in such cases the gastrointestinal lesions were mediated through the hypothalamus without its manifesting any morbid process. In reviewing simultaneous lesions of the brain and gastrointestinal tract, Davidoff[7] concluded that a lesion situated anywhere between the cerebral cortex and the medullary region might upset the gastric function in such a way as to produce acute ulceration. Zimmerman[8] recalls that in subsequent years Cushing was also convinced that gastric erosions associated with cerebral lesions sparing the hypothalamus might be attributed to involvement of the descending pathways. In view of the relative rarity of this condition, as well as the attendant surgical problems, we have considered it worth while to report a successful gastrectomy for acute gastric erosions associated with massive hematemesis and developing shortly after the onset of a cerebrovascular accident. As originally intimated by Cushing and more recently by King and Reganis,[9] successful operative treatment of neurogenic stomach erosions is most unusual.

On the basis of the literature it appears that the cerebral lesion, confined to the region of the internal capsule, may well account for the gastric erosions. This would be the interpretation of Zimmerman and

*From the departments of Surgery and Medicine, State University of New York Upstate Medical Center.

†Clinical assistant professor of surgery, State University of New York Upstate Medical Center.

‡Clinical instructor in medicine, State University of New York Upstate Medical Center.

other neuropathologists who have reported similar experiences. As suggested above, one can only speculate on the possible causal relation between the cerebrovascular accident described above and the acute bleeding gastric ulcers. Certainly positive proof is not at hand, despite the experimental production of similar gastric erosions by electric stimulation of the hypothalamus and higher centers of the brain.

Today, another school of thought has developed that would interpret the case reported below somewhat differently. Many authors have pointed out that acute gastrointestinal ulceration is seen as part of the body's reaction to stress. The philosophy on which the "stress ulcer" is based probably dates from Curling,[10] who in 1842 described acute ulceration of the duodenum in cases of burns. Penner and Bernheim[11] reviewed the literature and cited their own observation of acute peptic ulcer developing during periods of peripheral circulatory collapse. It is generally recognized today that a variety of noxious stimuli, including burns, wounds, surgery and shock, incite the adrenal gland to pour forth a hypersecretion of cortical hormone, as part of the "adaptation response." Furthermore, Gray and his associates[12] have shown that the administration of ACTH and cortisone cause a great increase in gastric acidity and gastric pepsin secretion. Sauer and his colleagues[13] have reported cases of acute gastrointestinal ulceration seen in the course of the clinical use of cortical steroids. Selye[14] has recently demonstrated experimentally that intense systemic stress or adrenocortical hormones may abolish tissue resistance to the digestive action of gastric juice. Therefore, if one subscribes to the Selye[15] school of thought, the case of hemiplegia reported below represents such an example of stress, and the acute gastric ulcers may have been causally related to the hypersecretion of cortical hormone incident to stress.

McDonnell and McCloskey[16] reviewed a long series of autopsied cases and found that acute peptic ulcers occurred as commonly in patients undergoing surgery (non-neurologic operations) as in patients harboring central-nervous-system lesions. They concluded, "It seems more than likely that the acute peptic ulcers that occur in association with surgical procedures, burns, intracranial lesions, etc. are simply one result of the body's exposure to stress." This was the interpretation of Salasin and Bowers,[17] who reported a successful gastric resection for acute gastric ulcers associated with hematemesis seen in the immediate period after a nephrectomy. The stress-ulcer philosophy, like the Cushing neurogenic thesis, remains speculative for the present.

Hume[18] has seemingly combined both schools of thought in what he terms the "neuroendocrine response to injury." It has been shown experimentally that the hypothalamus may be so damaged as to prevent the ACTH response to injury. Hume concludes that afferent stimuli arising from a stressful situation, which may exist anywhere in the body, reach the hypothalamus, which in turn elaborates a substance into the portal circulation of the anterior pituitary gland. The gland so acted upon then releases ACTH, which stimulates the adrenal gland to secrete cortical hormone.

Quite aside from these theoretical considerations about the pathogenesis of the acute gastric ulcer, one must consider some of the practical aspects of the management of a patient suffering recurring massive hematemeses. X-ray examination soon after admission of such patients to the hospital is being advocated in many centers today. Although this technic often discloses the correct diagnosis, the presence of retained blood clots in the stomach may obscure the actual disease, as in the case reported below, in which the roentgenologist believed that the hematemesis was caused by a gastric neoplasm. Massive hematemesis often originates from superficial gastric erosions, so shallow that their presence escapes detection not only by the radiologist but also by the operating surgeon. It therefore seems sound to perform a wide gastrotomy in cases of hematemesis in which the stomach presents no external abnormality. Such a policy would obviate the performance of a "blind gastrectomy" and its attendant undesirable sequela in patients harboring no organic lesion of the stomach.

Case Report

A 75-year-old unmarried woman was admitted to the Syracuse University Hospital on May 14, 1950, with a history of having suddenly lost consciousness while mowing her lawn. Her relatives stated that she had always been in excellent health except for high blood pressure. The patient had been remarkably free of any gastrointestinal symptoms before admission.

Physical examination revealed a confused, thin woman. Examination of the chest and abdomen was not remarkable. Considerable dysarthria was noted. Slight nuchal rigidity was present. The tongue protruded to the left. Neurologic examination disclosed a left-sided flaccid hemiplegia, with involvement of the face, arm and leg. The Babinski sign was present on the left. The reflexes in the left arm and leg were hypoactive.

The temperature was 100°F., the pulse 86, and the respirations 20. The blood pressure was 190/80.

Examination of the blood demonstrated a hemoglobin of 13.5 gm. per 100 cc., with a hematocrit of 40 per cent, and a white-cell count of 6600, with a normal differential and smear. Routine urinalysis and stool examinations were negative. An electrocardiogram showed a normal sinus rhythm with multiple atrial and nodal premature beats, as well as evidence of enlargement and strain of the left ventricle.

Two weeks after admission the patient was much improved. The picture of mental confusion had cleared, and she was beginning to move the previously paralyzed arm and leg. Her cardiac rhythm had reverted to normal.

Fifteen days after the cerebrovascular accident she complained of epigastric pain, passed several tarry stools, and went into a state of peripheral circulatory collapse. The systolic blood pressure was recorded at a level of 60. She was given plasma and whole-blood transfusions. During the next 7 days melena continued in association with repeated massive hematemeses of bright-red blood. During this 1-week period 7500 cc. of whole blood was administered, the hematocrit ranging between 21 and 38 per cent. The nonprotein nitrogen rose to 84 mg. per 100 cc. Two gastrointestinal x-ray series were performed during the acute bleeding period. The esophagus and duodenum were reported normal. The x-ray films were interpreted as showing a tumor mass in the stomach, possibly extramucosal in origin.

In view of the persistent hematemeses as well as the x-ray report of tumor, laparotomy was decided on despite the very poor general condition of the patient. Local and splanchnic novocain infiltration provided the anesthesia for the most part. No abnormality was apparent on exploration of the abdomen. The stomach presented no outward sign of tumor or ulcer. It was decided that a so-called "blind gastrectomy" was not warranted in such a poor-risk patient, and accordingly a large gastrotomy was performed. Four acute shallow gastric ulcers high up on the lesser curvature were then visualized. A Billroth I subtotal gastrectomy was performed, after which the patient recovered uneventfully, being discharged to a convalescent home on the 15th postoperative day.

Pathological examination of the subtotally resected stomach revealed no serosal abnormality. Four superficial ulcerations 1.0 to 4.5 cm. in diameter were present on the lesser curvature (Fig. 1). In the base of one of the ulcers a large submucosal artery was noted. Microscopical examination revealed multiple shallow ulcers whose floor contained necrotic material, fibrin, and degenerating leukocytes. The inflammatory reaction extended through the muscularis mucosae into the submucosa. Microscopical study demonstrated an erosion of the wall of a submucosal artery adjacent to the floor of one of the ulcers, with partial recent thrombosis (Fig. 2).

After discharge from the hospital the patient appeared to be progressing satisfactorily in a convalescent home. Her mental confusion and hemiparesis improved considerably. Suddenly, without warning, she became comatose about 2 months after the original cerebrovascular accident and died shortly thereafter.

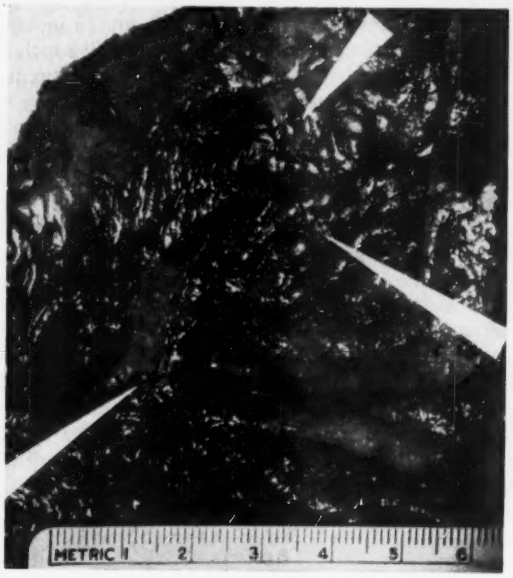

FIGURE 1. *Gastric Mucosa of the Partially Resected Stomach.*

Note the multiple superficial erosions as indicated by the white arrows.

Post-mortem examination disclosed no significant intra-abdominal abnormality except for evidence of a previous partial gastric resection. Gross and microscopical examination of the adrenal glands was not remarkable. Terminal bronchopneumonia was present. When the cranial cavity was opened an area of infarction was noted in both cerebral hemispheres confined to the insular regions—areas supplied chiefly by the middle cerebral artery. Severe arteriosclerosis of the vessels comprising the circle of Willis was observed. The area of softening on the right side represented a recent lesion and involved the region of the lateral ventricle extending through the internal capsule in its midportion. There was no gross evidence of pathologic changes in the hypothalamic region. In summary, it was the impression of the prosector that the bilateral areas of cerebral infarction were confined to the portions of the brain supplied by the middle cerebral arteries.

SUMMARY

A case of acute gastric erosions associated with massive hematemesis occurring in the wake of a cerebrovascular accident for which a successful gastrectomy was performed is reported. Autopsy at a later date showed that the cerebral lesion involved the internal capsule and areas of the brain supplied by the middle cerebral arteries. No pathologic changes in the hypothalamus were noted.

The pathogenesis of acute gastric ulceration occurring under such circumstances is discussed from the point of view of the "neurogenic-ulcer" thesis of Cushing as well as the "stress-ulcer" hypothesis of Selye. The clinical management of acute superficial gastric erosions may pose a serious surgical problem by virtue of massive hematemesis incident to erosion of sclerotic submucosal vessels, as in this case.

FIGURE 2. *Photomicrograph of a Superficial Gastric Erosion (X8).*

Note the eroded and partially thrombosed, good-sized submucosal vessels situated in immediate proximity to the floor of the ulcer.

We are indebted to Dr. Robert O. Gregg for assistance in the management of the case reported.

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EVALUATION OF THE CIRCLECUF FOR MEASUREMENT OF HUMAN BLOOD PRESSURE*

GEORGE P. FULTON, PH.D.,† DONALD I. PATT, PH.D.,‡ AND ELMER B. MODE, A.M.§

BOSTON

THE Circlecuf¶ (Fig. 1) is a new device for the indirect measurement of blood pressure in man. It differs in principle from similar instruments because of the distinctive property of a circumferential air bladder providing for the uniform application of pressure around the upper arm. Consequently, the Circlecuf is merely drawn over the arm like a sleeve and becomes "self-fitting" with inflation. This feature of the instrument makes it practical for self-measurement of blood pressure.

EXPERIMENTAL PROCEDURES

The Circlecuf was compared with a standard "wrap-around" cuff for blood-pressure measurements during "rest" in a group of 48 normal college students (32 men and 16 women). The subjects were seated for several minutes in a quiet room before measurement. Six successive determinations were made in pairs on each subject, the use of the Circlecuf being alternated with that of the "wrap-around" cuff. Consequently, a total of 288 blood-pressure readings (144 for each type of measuring device) were made. In 50 per cent of the subjects (24), the measurements were made in the following order: first, "wrap-around" on the right arm; secondly, Circlecuf on the right arm; thirdly, Circlecuf on the left arm; fourthly, "wrap-around" on the left arm; fifthly, "wrap-around" on the right arm; and, finally, Circlecuf on the right arm. In the remaining 50 per cent the order of the measurements was reversed. Similarly, the Circlecuf was compared with a standard "snap-on" cuff in a group of 30 students (22 men and 8 women).

FIGURE 1. *Circlecuf Blood-Pressure Measuring Unit (Courtesy of Robbins Instrument Corporation).*

The Circlecuf is manufactured in 5 sizes varying by 2.5-cm. (1-inch) increments from 24 to 34 cm. (9½ to 13½ inches) in maximum inside circumferences. The width of all sizes is 15 cm. (6 inches). In this study the size measuring 32 cm. (12½ inches) was used throughout except for 1 man (arm circumference, 33 cm.) and 1 woman (arm circumference 34 cm.), both requiring the largest size, and for small children, for whom the minimum size was selected. Over 95 per cent of the adult subjects could be fitted comfortably with the 32-cm. size.

For the purpose of limiting the comparison to the fundamental differences in principle inherent in the construction of the cuffs, the same gauge and valve were used throughout. In this way the probability of minor discrepancies attributable to valves and gauges was eliminated. A stethoscope was employed throughout for detection of the Korotkow sounds as criteria of the systolic and diastolic pressures. In accordance with the recent recommendations of Bordley et al.,[1] the complete cessation was taken as diagnostic of the diastolic pressure. This undoubtedly accounts for many of the low values obtained (Fig. 2 and 3).

RESULTS

Comparison of Circlecuf with "Wrap-around" Cuff in "Normal-Pressure" Range

The blood pressures as determined with the Circlecuf were consistently several millimeters of mercury lower for both systolic and diastolic values than corresponding pressures on the same arm as determined with the "wrap-around" cuff. A comparison of the results obtained with the two methods of measurement is shown in the scatter diagrams (Fig. 2-5).

In Figure 4, systolic blood pressures (mean values for two measurements) taken with the Circlecuf on the left arm of 48 subjects are plotted against corresponding pressures taken with the "wrap-around" cuff. The resulting scatter diagram indicates linear

*From the departments of Biology and Mathematics, Boston University.
†Professor of biology, Boston University.
‡Associate professor of biology, Boston University.
§Professor of mathematics and chairman, Department of Mathematics, Boston University.
¶Manufactured by the David Clark Company, Worcester, Massachusetts.

regression and high correlation ($r=0.90$). The equation ($y=4.1 + 0.93x$) shows the relation to be expected between corresponding blood-pressure readings. The differences (d) between each pair of readings on the same subject ("wrap-around" cuff minus Circlecuf, or x-y) were computed. The 95 per cent confidence limits for the mean differences (μ_d) were 2.0 to 5.5. Consequently, systolic blood pressures determined on the left arm with the Circlecuf are likely to be lower by 2 to 5 mm. of mercury than corresponding pressures determined with the "wrap-around" cuff.

Diastolic pressures taken with the Circlecuf on the left arm are plotted in Figure 2 against corresponding pressures taken with the "wrap-around" cuff on the same arm. Linear regression and high correlation ($r=0.88$) are evident. The confidence limits were calculated as 4.8 to 7.9. Consequently, diastolic blood pressures determined on the left arm with the Circlecuf can be expected to be lower by 5 to 8 mm. of mercury.

In Figure 5 systolic blood pressures (mean values for 4 measurements) taken with the Circlecuf on the right arm of the same 48 subjects are plotted against corresponding pressures taken with the "wrap-around" cuff on the same arm. Linear regression and high correlation ($r=0.91$) were again indicated. The 95 per cent confidence limits (2.1 to 5.0) show that systolic blood pressures determined on the right arm with the Circlecuf will probably be lower by 2 to 5 mm. of mercury than corresponding pressures determined with the "wrap-around" cuff.

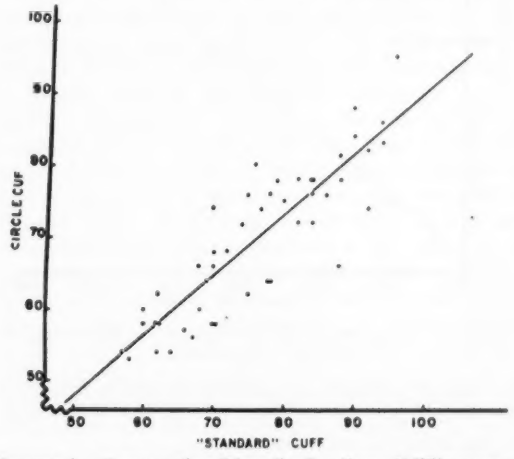

FIGURE 2. *Comparative Diastolic Readings (Millimeters of Mercury), Left Arm.*

Diastolic pressures taken with the Circlecuf on the right arm are plotted in Figure 3 against corresponding pressures taken with the "wrap-around" cuff on the same arm. The confidence limits (4.4 to 6.9) indicate that diastolic blood pressures determined on the right arm with the Circlecuf will probably be lower by 4 to 7 mm. of mercury.

No correlations were apparent between arm circumference (ranging from 21.6 to 31.3 cm.) and similarity of readings with the Circlecuf (32-cm. size) and the standard "wrap-around" cuff. The initial inflation of the Circlecuf appeared to be a "self-fitting" feature, and no variability attributable to fit could be detected.

Comparison of Circlecuf with "Wrap-around" Cuff in "Elevated Pressure" or Hypertensive Range

Obviously, the Circlecuf must perform as well in higher pressure ranges as in the "normal" range if it is to compare favorably with other devices. The scatter diagram of systolic pressures (Fig. 4) indicates linearity from 90 to 148 mm. of mercury. In the hypertensive range, Freis[2] made comparative measurements on 13 patients with "resting" systolic pressures ranging as high as 188 mm. Although the Circlecuf readings were slightly lower, no significant differences were apparent between values obtained with the two devices.

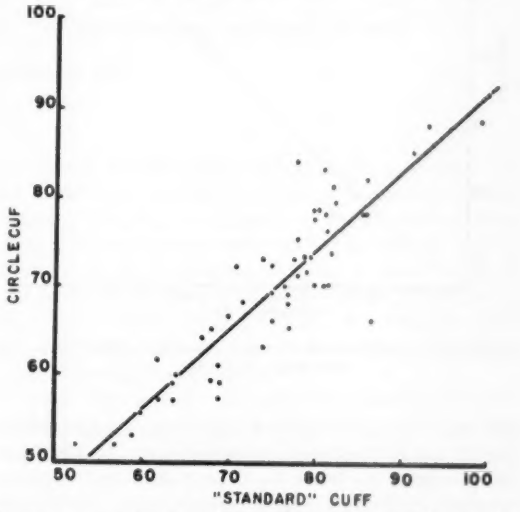

FIGURE 3. *Comparative Diastolic Readings (Millimeters of Mercury), Right Arm.*

Comparison for Use with Children

The Circlecuf (24-cm. size) was compared with the standard "wrap-around" cuff for a total of 18 blood-pressure measurements on 3 children (five, seven and eight years of age). Readings taken with the Circlecuf were slightly lower, as in adults. In the youngest child (arm circumference, 18 cm.) the readings obtained with the two instruments were almost identical. This may be explained by the fact that, owing to overlapping of the inflated portion, the standard "wrap-around" cuff becomes practically a "Circlecuf" when applied to a very small arm.

Comparison of Circlecuf with "Snap-on" Cuff

The systolic and diastolic blood pressures as determined with the Circlecuf were slightly lower by

several millimeters of mercury than corresponding pressures on the same arm as determined with the "snap-on" cuff. The 95 per cent confidence limits for the mean differences between the systolic readings were calculated as 2.9 to 7.1 for the left arm and 3.6 to 6.7 for the right arm. For the diastolic pressures, the confidence limits were 5.0 to 9.5 for the left

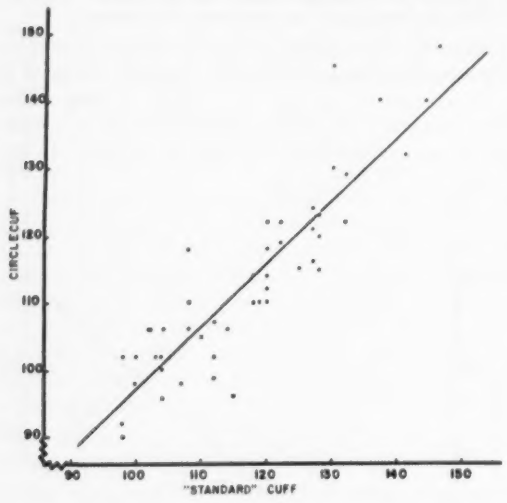

FIGURE 4. *Comparative Systolic Readings (Millimeters of Mercury), Left Arm.*

arm and 6.5 to 9.6 for the right arm. Consequently, systolic blood pressures determined with the Circlecuf will probably be lower by 3 to 7 mm. and diastolic pressures by 5 to 10 mm. of mercury than corresponding pressures determined with the "snap-on" cuff.

Self-Measurement of Blood Pressure

A total of 20 persons (5 women and 15 men), untrained in the measurement of blood pressures, were given brief instructions individually and simple demonstrations in the use of the Circlecuf for determination of their own pressures. After a few minutes of practice each subject ascertained his pressure twice, recording both systolic and diastolic pressures. One of the investigators then made 2 determinations on the subject, using the identical equipment.

Analysis of the data indicated that the readings made by the untrained subjects were comparable with those made by the investigator. No significant variations attributable to inexperience were found. The mean difference for systolic pressures was 4.3 mm., and that for diastolic pressures was 6.1 mm. In only 4 cases among 20, the differences exceeded 10 but not 15 mm. of mercury.

It can be concluded that self-measurement of blood pressure by inexperienced persons is feasible, provided that simple but adequate instructions are given, and that the Circlecuf is a practical device for this purpose.

Discussion

Certain basic recommendations concerning equipment and technics for the determination of human blood pressure by sphygmomanometry have been published by the Committee to Revise Standardization of High Blood Pressure Readings, Council for High Blood Pressure Research, American Heart Association.[1] The measurement of blood pressure by indirect methods with various kinds of sphygmomanometers has been shown to be in error by a mean value of ±8 mm. of mercury for both systolic and diastolic components, on the basis of comparisons with measurements by direct intra-arterial manometers. Auscultatory systolic values are 3 to 4 mm. of mercury too low on the average, and auscultatory diastolic values, particularly those taken at the "point of dulling of the sounds," are approximately 8 mm. too high. The theoretical reasons for the low systolic and high diastolic readings with blood-pressure cuffs are discussed by Bazett and his co-workers.[3,4] It is probable that the differences between the Circlecuf and the "wrap-around" or "snap-on" cuffs are explainable on

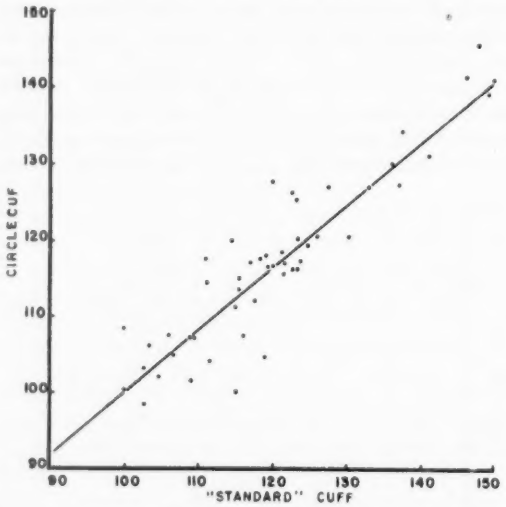

FIGURE 5. *Comparative Systolic Readings (Millimeters of Mercury), Right Arm.*

the basis of geometric or mechanical factors involving the distribution of air pressure on the upper arm during inflation and deflation.

The slightly lower values for systolic pressure (2-5 mm. of mercury) obtained with the Circlecuf have no practical consequence and are within the average scatter to be expected from variability. The slightly lower values for the diastolic pressure (4-8 mm.) are in a favorable direction, since erroneously high diastolic readings are reported to result from the usual types of blood-pressure cuffs.

Conclusions

The Circlecuf compares favorably with standard

"wrap-around" and "snap-on" types of sphygmomanometers for the measurement of human blood pressure. It has an obvious advantage in the ease of application to the arm. The Circlecuf (small size) is convenient for use with children. The slightly lower values obtained with the Circlecuf for both systolic and diastolic pressures have no practical significance.

The Circlecuf is a practical device for the self-measurement of blood pressure by inexperienced persons, provided that simple but adequate instructions are given.

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MEDICAL PROGRESS

RESUSCITATION AND OTHER USES OF ARTIFICIAL RESPIRATION

James L. Whittenberger, M.D.†

BOSTON

IN 1865, Sansom[1] summarized the state of the art of resuscitation as follows: "All existing facts, and all the latest experiments, point to the conclusions that there is only one perfect stimulus to the failing heart, the stimulus of a sufficiently aerated blood, and that the only mode of producing it is the excitation of respiration." Thus, resuscitation has long been equated with artificial respiration, though it may deserve a larger definition. Since most recent advances in this field have been in methods of artificial respiration this aspect of resuscitation will be considered particularly. Other important measures have been reviewed by Saklad,[2] Wiggin et al.[3] and others.[4-6]

Recent progress has been catalyzed by several factors: the growth of thoracic surgery, increasing numbers of poliomyelitic patients with respiratory paralysis and the need for more adequate methods to use in the event of nerve-gas poisoning. A comprehensive review of the literature in these fields is not attempted here. Major emphasis is on advances in knowledge of the physiologic characteristics of the lungs, the bearing of these characteristics on the action of methods of artificial respiration and the effects of the various methods on circulation and respiration. For excellent historical accounts readers with special interests are referred to books by Karpovich[7] on manual artificial respiration and Mushin and Rendell-Baker[8] on methods used in thoracic anesthesia.

Cardiorespiratory Failure

Development and use of therapeutic methods is always facilitated by knowledge of the disturbances in function of the systems treated. Swann and his associates[9-11] and others[12] have clarified understanding of the events in acute experimental respiratory failure. As is well known, the systems most susceptible to functional failure during asphyxia are the heart and the medullary centers controlling respiration; both systems, however, are capable of being revived, even after periods of severe asphyxia for as long as half an hour. This does not mean that the brain as a whole can survive such periods of asphyxia; if circulation to the brain is absent for more than a few minutes, local areas of permanent damage occur. This subject has been reviewed by Heymans.[13]

It has been stated that respiration usually fails first in response to acute anoxia, and that several minutes are available subsequently, during which artificial respiration should result in successful resuscitation.[14] Exceptions to this sequence have been emphasized by Swann and Brucer[15]; these authors found in unanesthetized dogs that circulatory and respiratory failure were likely to occur at about the same time in most types of anoxia, except carbon monoxide poisoning.

It is typical of severe anoxia that when respiration and circulation fail, they fail suddenly. The rapid decline of arterial pressure accompanying anoxic myocardial failure has been used by Swann et al.[16] as an end point in the evaluation of methods of resuscitation. In a large series of dogs an interval of only twenty seconds was found to separate the arterial pressure level at which all animals could be resuscitated and the pressure level at which no survivals occurred, regardless of the method of artificial respiration employed. The practical conclusion of these studies is the forcible re-emphasis of the fact that circulatory failure and death are the result of myocardial anoxia, and that any measure that restores an oxygen supply to the heart is a prime requirement of successful resuscitation; in acute asphyxia this result may be achieved by a single breath of fresh air. If the circulation has failed to the point where respired oxygen is not carried to the heart a direct attack, such as cardiac massage, must be instituted without delay.

The metabolic events in acute cardiorespiratory

*From the Department of Physiology, Harvard School of Public Health.

†Professor of physiology, Harvard School of Public Health.

failure have been re-examined by Swann and Brucer[10] and by Herber.[17] Their results substantiate those of Grodins, Lein and Adler[18] in portraying the metabolic changes as a respiratory acidosis followed by an increasing metabolic acidosis. Thus, further evidence has been added against the use of gas mixtures containing carbon dioxide in resuscitation.

Respiratory Mechanics in Relation to Artificial Respiration

The basic problems in artificial respiration are concerned with the altered mechanical characteristics of respiratory structures, how to adapt therapeutic methods to these alterations, how much ventilation should be provided and what effects methods of artificial respiration have on respiration, circulation and other functions of the body.

Until lately it has not been adequately appreciated how dependent the pulmonary ventilation is not only upon the method employed but also upon the qualities of the lungs and thorax. Recently, improved methods have provided increasing knowledge of the mechanical behavior of the lungs and thorax.[19-22] Although direct observations on the lungs of acutely apneic patients are almost nonexistent, fairly reliable predictions from data in laboratory animals appear warranted.

The pressure-volume relations of respiratory structures have static and dynamic components; when air is not flowing, lung volume is related to tissue elasticity, gravity and other static factors. This relation, expressed as liters of volume change per centimeter of water static-pressure difference "across" the lungs or lungs and thorax, has been called compliance.[22] A *more compliant* lung has a greater volume change when a unit of force is applied.

In the lungs of a newborn baby,[23] in a lung collapsed during thoracic surgery,[24] and in the presence of pulmonary edema surface tension plays an especially important part in compliance. Lungs that have become essentially airless require much more pressure for inflation than they do for ventilation once they have been fully inflated. This phenomenon accounts, in part at least, for the fact that the newborn baby's first breaths are its hardest ones; it may also account for some of the inconsistencies in the literature on resuscitation of the newborn.

Partly by means of the surface-tension effect several pathologic conditions of the lungs affect compliance. Pulmonary vascular engorgement, hemorrhage, edema, consolidation, atelectasis and other diseases that lower the number of functioning alveoli will reduce the compliance, and consequently increase the pressure variations required for adequate aveolar ventilation.[25,26] Although few measurements of distensibility have been made in apneic patients, the prevalence of pulmonary edema and other types of pathology in such cases strongly suggests that decreased compliance of the lungs is a frequent handicap in artificial respiration.[7,27]

The behavior of lungs in which surface tension markedly affects compliance has implications in artificial respiration. Drinker[28] observed a gradual decrease of distensibility of the lungs of anesthetized dogs that breathed quietly for several hours in a fixed recumbent position. At autopsy the lungs showed severe congestion and slight edema of the dependent portions; inhalation of aerosolized dye disclosed that the involved parts were not ventilated.[29] It is my experience that these changes can be prevented by occasional maximal inflation of the lungs. It has also been a consistent observation that compliance of the lungs can be temporarily increased by a single overinflation.[25] These facts add support to the idea that methods of artificial respiration should, if possible, include a means of providing an occasional deep breath.

The second component of force required to ventilate the lungs is that causing flow; this constitutes the "dynamic" portion of the intrapleural-atmospheric pressure difference. The pressure drop in the air passages and "across the lung" during air movement is related to frictional losses from air flow and sliding of tissue elements on each other. In normal air passages resistance is low, but it may be very high in asthma, laryngospasm or any other form of obstruction in the airway. The importance of having a clear, unobstructed airway in artificial respiration is apparent. If a patient is being made to breathe by a constant pressure wave slight changes in resistance that are due to airway secretions may make a large difference in the ventilation achieved.

The mechanical attributes of the lungs not only control the ventilation achieved by a method of artificial respiration but also modify the circulatory phenomena accompanying the method. Thus, a high resistance in the airway reduces the fluctuations of alveolar pressure that would otherwise occur in response to a given mask pressure pattern; consequently, there would be less variation of intrapleural pressure. A reduction of lung distensibility would similarly decrease the fluctuations of intrapleural pressure in response to a given mask pressure pattern.

Although the thoracic walls as well as the lungs are moved by almost every form of artificial respiration, little is known about the force required to move the thorax itself. Up to a level of lung volume well above the resting end-expiratory position, the elastic elements of the thorax act to enlarge its volume, in opposition to the retractile force of the lungs; the lungs collapse when air is admitted to the pleural space, whereas the thorax expands.[19] As the lungs are inflated by rising pressure in a face mask the intrapleural pressure rises also, and at some point equals atmospheric pressure; the thoracic volume at this point corresponds to the relaxation position of the thorax, and above this volume some portion of the mask pressure is required to distend the thorax.

Ventilation Control During Artificial Respiration

From the variability of pulmonary characteristics in patients requiring artificial respiration it follows that a given appliance at a fixed setting will provide widely different alveolar ventilation rates in various persons and even in the same person at different times. In the absence of an intact respiratory control mechanism in the patient there is no precise way of relating pulmonary ventilation to the metabolism of the body. Frequent sampling of arterial blood for pH determination would be a sound guide but is impractical. Monitoring of alveolar carbon dioxide tension is more nearly feasible, but equipment for this purpose is expensive. As a practical guide, based on ventilation measurements and the patient's body weight, Radford et al.[30] have devised a nomogram for predicting the desired tidal ventilation at a given rate. This method has given promising results in guiding the care of convalescent poliomyelitic patients in respirators.

Safe Levels of Intrapulmonary Pressure

While properties of the lungs are being considered note should be taken of the limits of pressure that can be safely applied. Despite many attempts a satisfactory study of this problem has not been reported. Incorrect analogies have been made between pressures used in artificial respiration and those attained during a natural cough or during forced respiratory efforts against a blocked airway.

Alveolar rupture and interstitial emphysema result from tissue stretch rather than the absolute levels of pressure in the thorax. Thus in a cough intra-alveolar pressures exceeding 100 mm. of mercury may be obtained[31] but coughing has not been recognized as a cause of pulmonary rupture. As expiratory muscles are tensed during a cough the volume of the lungs is actually diminished, and the pressure levels throughout the chest go up simultaneously; the *pressure difference* between alveoli and intrapleural space is not increased, and consequently lung tissue is not stressed. The pressure difference affecting the lung tissue is a function of the depth of inspiration before coughing — in other words, of the volume of the lungs.

In the range of the vital capacity of most human beings the maximal pressure difference related to compliance (static pressures) probably seldom exceeds 30 mm. of mercury.[32] Until more information is available this may be taken as a safe level of pressure applied statically to the lungs within the chest. A slightly lower value would be advisable for lungs in an open chest, but an exact figure cannot be given.

If a pressure of 50 mm. of mercury were applied statically to the lungs of a patient three results could occur. If expiratory muscles were reflexly or voluntarily tensed lung inflation would be limited, and the applied pressure would have only the circulatory effects of a Valsalva maneuver. If the patient had respiratory paralysis lungs and thorax would be distended until the pressure difference across them equaled 50 mm. of mercury; at this time much more than half the pressure would be distending the lungs, and alveolar ruptures might occur. Lastly, if the patient assisted the pressure by active inspiration, his lungs would be stretched even more, and alveolar trauma might be severe. Since these possibilities have not been taken into account in published studies a quantitative evaluation of safe pressure limits for respiratory devices is not possible. Most respirators, resuscitators and automatic machines for controlled respiration in anesthesia do not inflate the lungs beyond a volume corresponding to 15 or 20 mm. of mercury pressure. Some positive-pressure breathing devices and an exsufflator[33] are capable of developing inspiratory pressures up to and in excess of 30 mm. of mercury. Presumably, patients subjected to excessive inflation pressures protect their lungs from overexpansion by reflex tensing, for no evidence of damage from these devices has yet been reported.

Methods of Artificial Respiration

For practical reasons it is justifiable to divide the methods into those for use in a true emergency and those suitable for more or less prolonged artificial respiration. Only two qualify as true-emergency procedures, except in an operating room or similarly prepared location, where any method may be available for emergency use; those requiring no equipment are the manual and the mouth-to-mouth insufflation methods.

Pertaining as it does to all methods, the fact should be emphasized that the single most critical consideration in any method is the patency of the upper airway; it is clearly impossible to aerate the lungs if the upper airway is blocked. Establishing a clear airway involves proper position of the head, tongue and jaw, use of gravity to promote drainage and adequate aspiration of secretions when necessary. These are matters that require skill, preparation and training.

Manual Methods

Until 1948 the Schäfer prone-pressure method was most widely taught in the United States, although, as pointed out by Comroe and Dripps,[34] there was little quantitative evidence to support the generally held opinion of its value. Several authors have attempted to evaluate manual methods in human subjects after death, with little or no success; with the use of Schäfer's method this has been attributed to loss of elasticity at the time of death. Since such a loss of elasticity was not found by Whittenberger et al.,[35] some other explanation must be found for the changes in response that occur after death. Durlacher, Banfield and Bergner[36] found that progressive transudation of fluid into the lungs of dogs occurred after death; the resulting change of compliance, if

it occurred in man, could account for failure of the Schäfer method.

In 1950 Gordon and his associates[37] presented the first comprehensive evaluation of several methods in fresh corpses. Most striking was the relative success of methods that had an active inspiratory as well as an active expiratory phase; these included the Nielsen, or back-pressure arm-lift method, and the back-pressure hip-lift method. The Nielsen method, though described in 1932, had not attracted much attention in the United States, and the hip-lift method, described by Thompson in 1935,[38] was apparently forgotten until rediscovered by Emerson in 1948.[39]

Sponsored primarily by the military services a coordinated program of research was carried on by several institutions, leading, in 1951, to an unusual degree of agreement on the efficacy of manual methods.[38,40-49] These studies included the large-scale use of anesthetized, curarized human subjects by Gordon and his associates.[40-43] The principal conclusions were that tidal ventilation due to back pressure alone was much smaller than that obtained when arm lifting or hip lifting was interposed between applications of back pressure, the ratio of tidal volume to dead-space volume thereby being much improved; the arm-lift method could be performed by one operator for long periods without excessive fatigue. In apneic human subjects[43] the combined technics were capable of maintaining normal arterial oxygen saturation, whereas dependence on the Schäfer method resulted in severe cyanosis within a few minutes. Arterial saturation values as low as 42 per cent were found, even though tidal and minute ventilation rates were numerically adequate; this association suggests that a severe abnormality of distribution of ventilation occurred when volume changes were restricted to the expiratory reserve compartment of the lungs.

The back-pressure arm-lift method has now been widely accepted for general use. The hip-lift technic, though requiring much more strength and endurance in the operator, has much merit and is being used as an alternative or preferred method by some rescue organizations; its advantages are that the upper airway can be observed more easily and it can be used in the event of upper-extremity fracture.

It is now apparent that there are several good procedures. The Silvester technic, another active-inspiratory-active-expiratory maneuver, is also effective and is preferred when the patient must remain supine; this position has the disadvantage of predisposing to upper airway obstruction. One of these, or the mouth-to-mouth method, is always available for emergency use. Applied speedily and properly they can save lives if there is a chance of revival.

Whether manual methods have a place in resuscitation of the newborn is not established. Certainly, pressure on the chest can accomplish little if there is no air in the lungs. Whether an active inspiratory maneuver can develop sufficient force to start inflation of airless lungs is not known.

(To be concluded)

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MEDICAL INTELLIGENCE

PNEUMATOSIS CYSTOIDES INTESTINORUM

Report of a Case Confirmed by Sigmoidoscopic Biopsy

NATHAN KREEGER, M.D.,*
AND LEON LITTMAN, M.D.†

BROOKLYN, NEW YORK

SINCE the first report of pneumatosis cystoides intestinorum hominis by Bang[1] in 1876, there have been over 250 case reports in the American and foreign literature. Hahn,[2] in 1899, recognized the similarity between this disease and one in hogs, and first applied the name pneumatosis cystoides intestinorum.

In 1952 Koss[3] presented a comprehensive review of the subject. He noted that the disease is three and a half times more frequent in males than in females and has its highest prevalence in the third, fourth and fifth decades. The etiology has never been firmly established, although most authors believe that gas in the lymphatics is the immediate cause of the disease. There are two major theories to explain the origin of this gas. One is that, as a result of pyloric stenosis secondary to peptic ulcer, air is forced into lymphatics that have been opened by the ulcerative process. This theory however, does not explain the so-called primary disease—cases not associated with peptic ulcer. The second theory, more generally accepted, postulates a chemical deficiency, possibly dietary in origin, which results in gas, which is produced either directly within the lymphatics or within the intestinal canal, and is

A

B

FIGURE 1. *Roentgenographic Studies.*

A = barium-enema examination, demonstrating an irregularly narrowed lumen, with large air spaces surrounding the barium-filled sigmoid. B = evacuation film, showing reticulated appearance of the sigmoid colon, with large air spaces outlined by the columns of barium.

*Clinical instructor in medicine, New York State University College of Medicine at New York; adjunct in medicine, Jewish Hospital of Brooklyn; associate in medicine, Jewish Sanitarium and Hospital for Chronic Diseases.

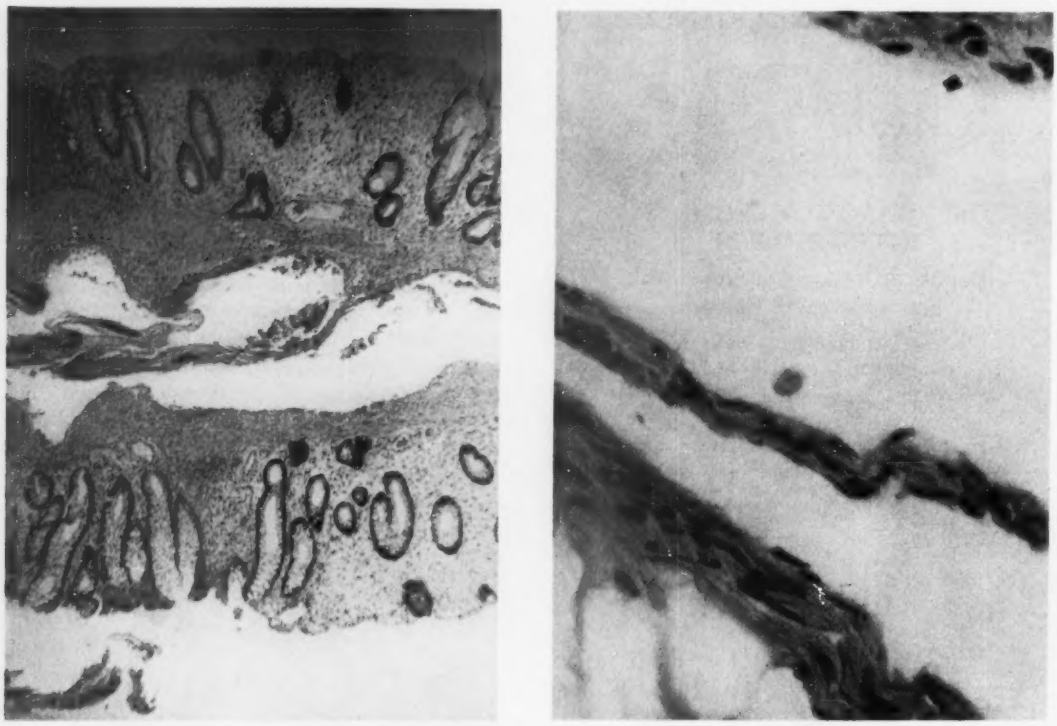
†Associate in proctology, Jewish Hospital of Brooklyn; proctologist, U. S. Naval Hospital, St. Albans, New York.

then absorbed into the lymphatics because of increased permeability of the mucosa.

In over 85 per cent of reported cases the disease has been associated with some other gastrointestinal abnormality, chiefly peptic ulcer with pyloric stenosis. Most pyloric lesions are associated with cysts of the small intestine whereas most large-bowel cysts are primary and with most of the cysts in the large bowel submucosal lesions are the rule. Villaume[4] has stated that cysts localized to the sigmoid are very uncommon.

Pathologically, two types of disease are recognized: the subserosal and the submucosal. In both, the gas-filled cysts are thin walled. The microscopical pathology of the cysts varies with their age. In the early stages they are lined with endothelial cells, which later coalesce to form multinucleated giant cells. In time these giant cells are sloughed off, leaving the cyst without any lining. At times inflammatory changes may be found surrounding the cyst. These may vary from acute changes, with infiltration by leukocytes, to the formation of granulomas, with epithelioid and giant cells.

The usual presenting symptoms are those of the associated disease—that is, peptic ulcer with pyloric stenosis—although there is occasionally a palpable abdominal mass. Diarrhea is seldom reported. Recently, much attention has been paid to the reticulated appearance of the bowel on roentgenograms.



A B

FIGURE 2. *Photomicrographs of the Specimen.*

A=*mucosa of the colon, showing cystic spaces and distended veins (hematoxylin and eosin stain x100).* B=*cyst wall lined with flat and low cuboidal cells (hematoxylin and eosin stain x300).*

CASE REPORT

S.R., a 60-year-old male office worker, has been followed by one of us (N.K.) since 1947. He has diabetes mellitus, which is controlled by diet, and arteriosclerotic heart disease with congestive failure, which has been well controlled with digitalis, ammonium chloride, Mercuhydrin and a low-salt diet. The only other medication used is chloral hydrate at bedtime for insomnia. Gastrointestinal roentgenograms taken in August, 1953, were interpreted as normal, including a 24-hour film in which barium had progressed to the mid-transverse colon.

On October 26 he passed bright-red blood by rectum. Examination revealed internal hemorrhoids. Sigmoidoscopic examination to a distance of 20 cm. was negative.

In January, 1954, he began to have diarrhea, which at first responded well to paregoric. However, during the next 3 months, there was alternating diarrhea (without bleeding) and constipation. Roentgenograms of the colon taken on April 21 showed numerous areas of increased translucency extending along the entire left side of the colon. The lumen of the bowel was irregularly narrowed by these filling defects, and air shadows were present on each side of the bowel (Fig. 1). The postevacuation study disclosed moderate emptying of the sigmoid loop and an irregular, giant-cobble-stone pattern.

On April 26 sigmoidoscopic study (by L.L.) was performed for a distance of 23 cm. Beginning 11 cm. from the pectinate line and extending to the 23-cm. level, cystlike globular masses protruded into the lumen in a scalloping manner, par-

tially occluding it, so that further passage was possible only by use of a narrow-bore scope. The mucosa covering these cysts was pale and tense and seemed fixed. About 14 cysts were visualized, varying from 0.5 to 3.0 cm. in diameter. A biopsy was taken from the lowermost of these lesions. The wound that resulted appeared honeycombed and did not bleed.

The pathological report was as follows:

The mucosa is everywhere well preserved. Within the submucosa there are large cystic spaces lined by flat or low cuboidal cells. Distended veins are also present. The picture is that of pneumatosis intestinalis and telangiectasis (Fig. 2).

At present the patient's cardiac and diabetic status are stabilized. Intermittent diarrhea is still present, but is fairly well controlled with paregoric and a low-residue diet.

Summary

A case of primary pneumatosis cystoides intestinorum is described in which the presenting symptoms were those of alternating diarrhea and constipation. The duration of the disease is known to be less than seven months. The etiology has not been determined, and one can only theorize concerning the causal relation of the sigmoidoscopic examination[5] in October, 1953, or the role of the various medications that the patient has taken over the past year.

We believe this to be the first case in which the diagnosis, made first by roentgenography, has been confirmed by a biopsy performed by sigmoidoscope.

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DOCTORS AFIELD

Ernest Gruening

James Howard Means, M.D.

BOSTON

A DOCTOR far afield from the medical point of view, but very far from afield in the career he finally elected to follow, is the Honorable Ernest Gruening, M.D., LL.D., journalist, public servant and statesman.

Gruening was a member of the Harvard College Class of 1907 and of the Harvard Medical School Class of 1911. Actually, he left the Medical School in the middle of his fourth year to take a job as cub reporter for the *Boston American*. Then and there he switched careers from medicine to journalism, or as he put it himself, he "decided to give up one profession for another, and exchange the art of curing the ills of the human body for an attempt to play a similar part in relation to the body politic." As it has turned out, these were prophetic words for he has indeed, throughout his life, played with distinction the role that so early he indicated. In spite of his change in objective, however, he returned to the Medical School long enough to earn his M.D. degree, which was granted him at Commencement in 1912.

Returning directly to his newspaper work he signed up, this time with the *Boston Herald*. It is interesting that, although he said, "it is always a good plan to start with Hearst in the newspaper game," he did not stay in that controlled environment very long. It was not one that his independent and forthright spirit could tolerate.

On the *Herald* he advanced rapidly through the various gradations of newspaper work until July, 1914, found him acting city editor of the *Herald* and November of that year managing editor of the *Boston Traveler*, which had then become the *Herald's* evening edition.

He served in this last-mentioned job for two years, and of it he had these significant remarks to make:

> It was an interesting job. The times were thrilling (World War I prior to U.S. participation); circulation, that summum desideratum of newspaper publishers, came readily. The only problems were those common to many American newspapers — to try to make the management understand that a newspaper owes very definite obligations to its readers — to the public — and that advertisers are entitled to the space they buy and not to special favors and considerations in the shape of suppression and distortion of news; that, in short, independence and intellectual honesty are the best policies.

If the press of the United States had had the ability or the desire to approach these high standards the country might be happier and better today.

In October, 1916, Gruening made a startling exposure of certain shocking "shenanigans" going on in City Hall, Boston, over the censoring of plays, and thus earned the enthusiastic approval of the editor of the *Herald*. The wounded, however, were so exalted politically that the owners of the *Herald-Traveler* ordered the publication of a retraction, and since Gruening would have no part in such ignominy, he resigned.

He went next to the *Boston Journal*, then a moribund paper, and together with a small group of friends, attempted to keep it alive. Some progress was made, but uncontrollable circumstances proved too difficult, and the paper failed. Gruening next took a whirl as managing editor of the *New York Tribune*, and after that he did his bit by enlisting in the field artillery.

After the war he managed *La Prensa* in New York —the only Spanish-American paper in the United States—for a year and a half—and then shifted for the first time to weekly journalism by becoming managing editor of the *Nation*, a post that he held for three years.

During this period he became conscious of, and strenuously opposed to, United States imperialism in the Caribbean. Under his direction the *Nation* brought to light certain facts about the unjustifiable

military intervention in Haiti in 1915 and in the Dominican Republic in 1916. In consequence of this exposé a Senate Commission of Inquiry was sent to the island in 1921, and Gruening was invited to accompany it. The findings of the Commission led to the withdrawal of United States forces from the Dominican Republic in 1924 and from Haiti in 1932.

In 1923 Gruening began a study of Mexican affairs, paying four visits to that country in as many years, and one to Spain for background. In 1928 the results of his studies appeared in his book, *Mexico and its Heritage.*

Two other newspaper items should be mentioned. In 1927 he was invited by a group of citizens of Portland, Maine, where, as in many other places, existing newspapers were quite under the control of business and political interests, to start for them an independent paper and to become its editor. He accepted this challenge. Its name was the *Portland Evening News,* and he kept it going until 1932. Then, however, as with many fighting independent newspapers, the financial odds were too great, and it had to be discontinued.

Gruening next went back to the *Nation* for a year, this time as editor, and finally wound up his journalistic career with a three months' fling as editor of the *New York Post.*

In 1934, for the second time in his life, he made a major change in career. This time he switched from journalism to the public service of his country. President Roosevelt, in the fall of 1934, appointed him director of the newly created Division of Territories and Island Possessions of the Department of the Interior.

The function of this new agency was to combine into one organization the affairs of territories and insular possessions that had formerly been scattered through several agencies. It included the Virgin Islands, Puerto Rico, Alaska and Hawaii. Gruening put his heart into this work and visited and studied all the areas within the jurisdiction of his division. The overcrowded and poverty-stricken state of the people of Puerto Rico particularly aroused him. Observing the simple fact that the population of this island was increasing faster than the food supply, and with scant funds available to import food, he made attempts both at industrialization and population control through education.

In 1939 Gruening was appointed governor of Alaska, and he served in that vital post until 1953. Directly after his appointment Alaska became of immense military importance. In 1940 the Governor obtained for the first time the establishment of a National Guard, and when this was federalized, he organized a territorial guard that had units scattered over the entire territory. From the beginning of his experience there, Gruening had great faith in Alaska. For years he has worked continually for its statehood. Recognizing its strategic importance, he believes that it would be a stronger outpost for the United States if it had the larger population and resources that statehood would give it.

There can be no doubt of the great usefulness of Ernest Gruening's life. He has always fought for the freedom of the press and has striven to improve the lot of the common man. In him the virtues of courage and sincerity are combined with keen insight into public affairs. It is for this reason that he may properly be called a statesman.

The readers of a medical journal will at once ask, Were his four years in medical school wasted, either for him or for the school? The costliness of medical education is such that it is usually an economic misfortune when a person who has earned a medical degree forsakes medicine. In Gruening's case, certainly this is not true. For himself, he has more than once stated that he has found his medical education constantly of value to him. It has given him understanding of the role of health in human welfare, and of how it can be promoted, that he would otherwise have lacked. The medical school can take satisfaction in having contributed to the education of a man who has served the country so well and will continue to do so, for his career is by no means finished. It is known, for example, that his book, *The State of Alaska,* will be published this autumn. This will, no doubt, be the definitive work on the Territory and Uncle Sam's relation to it during the eighty-seven years in which it has been his stepchild.

CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 40441

PRESENTATION OF CASE

A thirty-year-old woman entered the hospital because of abdominal pain.

The patient had been well until about six to eight months before admission, when she began to have "green-apple" cramps in the abdomen. The pain occurred at any time of day or night, was not related to meals and was not relieved by food, eructation, the passing of flatus or defecation. It gradually increased in frequency in the preceding three months, and during the past two or three weeks, she had had almost constant abdominal cramps and right-lower-quadrant tenderness. The bowel movements were normal until seven to ten days before admission, when they increased to two or three times a day; the stools became loose, and occasionally contained mucus. There was no nausea, vomiting, bloody stool, chill, fever or weight loss. Two barium-enema examinations done elsewhere revealed some obstruction in the region of the cecum (Fig. 1).

An appendectomy had been performed eighteen years before admission, and she had had three normal deliveries in eight years of marriage. For the past few years she had been "emotionally upset" because of domestic problems.

Physical examination showed a well developed and well nourished woman. The lungs were clear. There was a Grade 2 systolic murmur at the right base transmitted to the neck and apex. The abdomen was soft. There was a tender, firm mass about 2 by 3 cm. in the region of the old appendectomy scar. The right kidney seemed slightly enlarged and moved with respiration.

The temperature was 100.2°F., the pulse 96, and the respirations 22. The blood pressure was 120 systolic, 80 diastolic.

Urinalysis disclosed clear acid urine, a specific gravity of 1.032, and a ++ test for albumin, with 80 red cells, 5 white cells and 6 epithelial cells per high-power field in the sediment. Examination of the blood revealed a hemoglobin of 12 gm. per 100 cc. and a white-cell count of 8000, with 76 per cent neutrophils. The sedimentation rate was 46 mm. in sixty minutes. The stool guaiac test was negative. A roentgenogram of the chest was normal. The gastrointestinal and small bowel series demonstrated a normal esophagus, stomach and duodenal cap. In about seventy minutes the barium reached and filled what

FIGURE 1. *Barium-Enema Examination, Showing Contraction and Deformity of the Cecum.*

appeared to represent a much shrunken cecum. The exact location of the ileocecal valve could not be ascertained. The small bowel was not dilated, and no definite evidence of disease in the terminal ileum was observed. Barium-enema examination showed rapid filling throughout the colon to the midascending portion, where obstruction to the retrograde flow was met. Beyond this point a minute trickle of barium filled a small pocket, with constant configuration, overlying the ileum. Proximal to this the colon was suggestive of intussusception (Fig. 1). The terminal ileum was never filled. An intravenous pyelogram was not remarkable. Calcified areas, probably representing lymph nodes, were also present on the right side of and in the lower part of the abdomen.

The temperature came down to 98.8°F. on the second hospital day and remained normal thereafter. On the fourth hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. PERRY J. CULVER*: Since the x-ray films

*Assistant physician, Massachusetts General Hospital.

seem to be the one thing that might give me a clue to the nature of the process in the right lower quadrant I should like to examine them. Did the x-ray films of the chest show any dilatation of the aorta?

DR. JOHN F. GIBBONS: No; the aorta is normal. The films of the barium-enema examination all demonstrate a redundant colon, with a point of sharp narrowing at the cecal area and lowermost portion of the ascending colon (Fig. 1). The lumen of the bowel is markedly shrunken, contracted and irregular. In the evacuation films there seems to be a rounded mass superimposed on some air, which is probably in the distal tip of the proximal cecum. In the spot films of this area taken before evacuation, there is a suggestion of intussusception — that is, there is a very sharp cut-off between the normal and the abnormal portions of the lumen; the abnormal portion seems to disappear into that area, and there are concentric rings of bowel wall suggesting some telescoping of the cecum upward. There is a suggestion that this portion of the colon overlies and envelops the abnormal part. The small-bowel examination fails to reveal small-bowel disease; the pattern seems normal throughout. On the film made seventy minutes after the barium meal the head of the column is in the contracted portion of the cecum. Apparently, under the fluoroscope, there was no evidence of disease in the terminal portion of the ileum although in this film I cannot see that area clearly. The lesion is contracting the cecum and making it look irregular and is tending to intussuscept upward.

DR. CULVER: Do you think there is any ulceration?

DR. GIBBONS: No; I cannot find any ulceration. Actually, the mucosa in the contracted portion is not irregular and does not suggest an ulceration.

DR. CULVER: The air pattern in the terminal cecum underneath the narrowed shadow of barium bothers me.

DR. GIBBONS: The tip of the cecum does not fill as completely with barium as it does with air, but even the air pattern reveals a definite contraction of the lumen.

DR. CULVER: The liver is not enlarged?

DR. GIBBONS: No.

DR. CULVER: Calcified areas probably representing lymph nodes were said to be present on the right side in the lower abdomen. Is there any possibility that they were ureteral stones?

DR. GIBBONS: I do not see any. The shadows referred to are not in the path of the ureter.

DR. CULVER: I assume that "green-apple" cramps mean colicky cramps because later the patient began to have almost continual cramps. Did they occur in waves?

DR. RICHARD B. COHEN: They occurred at any time of the day or night. No more information was given.

DR. CULVER: Where were the cramps?

DR. COHEN: They were generalized.

DR. CULVER: Dr. Chester M. Jones teaches an important point — namely, that whenever a case is confusing, one should spend time trying to have the patient localize the pain exactly, with one finger if possible. Obviously, in this case that is impossible.

DR. HERSCHEL D. COLLINS: The pains were usually in the right lower quadrant.

DR. CULVER: Were they above as well as below the umbilicus?

DR. COLLINS: Yes; at one phase they were.

DR. CULVER: In other words they were not specifically large-bowel or small-bowel cramps?

DR. COLLINS: No.

DR. CULVER: Do you know anything about the patient's menstrual history?

DR. COHEN: Menses occurred every twenty-one to twenty-seven days, with dysmenorrhea throughout a seven-day period. She had had no intermenstrual bleeding and no discharge.

DR. CULVER: What was the date of the last menstrual period in relation to the urinalysis? I am looking for an explanation for the hematuria.

DR. CLAUDE E. WELCH: She was menstruating at the time the urinalysis was done. Later in the course the urine was normal.

DR. CULVER: The touch of the hand sometimes gives one a clue to the nature of a lesion. This mass was described as 2 or 3 cm. in size in the region of the old appendectomy scar. Was it in the abdominal wall, or was it deep and in the same area as the x-ray film shows it?

DR. COLLINS: It appeared to be in the same area as the mass noted in the x-ray film.

DR. CULVER: It seemed to be deep in the abdominal wall.

This patient had a history of abdominal pain, increasing in severity, of seven or eight months' duration. The pains apparently were colicky, which means that they were due to some process in a viscus. The x-ray films indicated that the ileocecal area was involved. I have to decide whether there was a generalized disease that could produce hematuria and possibly was related to the present episode. I had considered tuberculosis, which can produce hematuria, a lesion in this area and splenic enlargement. This disease still has to be kept in mind.

More specifically, I shall consider localized lesions in this area of the gastrointestinal tract. The Radiology Department has raised the question of intussusception. Intussusceptions occur in this area of the gastrointestinal tract most often, of course, in infants. In adults an intussusception usually starts on the basis of a polyp at the ileocecal valve. A Meckel diverticulum or cancer in the region of the cecum may start it. The fact that there was no bleeding — the stools had been guaiac negative — disturbs me. Intussusception of this duration and degree should have produced enough congestion of the involved bowel to cause some bleeding. I can almost imagine, however, that in this particular film, which shows a tiny neck of barium with some air beneath it, there is an intussuscepting diverticulum, but I think that is unlikely.

A localized ulcerative process on the right side of the colon is a possibility with that particular type of lesion. There is usually blood in the stool and fever. Abdominal cramps may be a symptom, but are not usually as prominent a symptom as in the more generalized type of ulcerative colitis; moreover, with right-sided ulcerative colitis I should not expect so much narrowing of the bowel.

Amebiasis is another explanation for a narrowed, shrunken cecum. There were no stool studies to rule out amebiasis. Amebiasis can be found without blood in the stool. The only point that bothers me is the constant pattern in the x-ray film — the trickle of barium and the dilated air-filled cecum around it.

A very rare condition that should be considered is hypertrophic tuberculosis, about which I know very little. It is a lesion that can involve the ileocecal valve and narrow the cecum; it is usually primary at the ileocecal valve without any lung involvement and can be relatively slowly progressive. Those features, together with the enlarged spleen and the history, make me want to consider the possibility of hypertrophic tuberculosis.

Cancer of the cecum is a rare condition in a person of thirty. If the patient had cancer of the cecum of this extent, I should expect some necrosis, with bleeding. Cecal cancers are notorious for producing severe anemia and bleeding. Because there was not a marked anemia, the guaiac reaction on the stool was negative and the patient was thirty, I shall not consider cancer.

Could this have been an inflammatory mass around the cecum, such as one might find with perforation from a regional ileitis? This patient was in the age group in which regional ileitis develops, and the history was certainly consistent. The only feature that bothers me about the possibility is the fact that nothing was seen on the small-bowel films; the terminal ileum was reported to look normal, and I hesitate to make that diagnosis.

If I had seen this patient clinically, I believe my next move would have been to call a surgeon because obviously this lesion was going to require exploration. I should simply put the possible diagnoses down on pieces of paper and put them into a hat. I should guess that this was hypertrophic tuberculosis and, as second choice, amebiasis.

A Physician: What about a carcinoid?

Dr. Culver: I thought of carcinoid when I thought about cancer. Perhaps this was carcinoid or cancer of the cecum, but I doubt it.

Dr. William Baker: Would you consider lymphoma?

Dr. Culver: I suppose one always has to consider lymphoma.

Clinical Diagnosis

?Tuberculosis.
?Lymphoma.

Dr. Perry J. Culver's Diagnosis

Hypertrophic tuberculosis of cecum.

Anatomical Diagnosis

Regional enteritis.

Pathological Discussion

Dr. Cohen: Dr. Welch, would you tell us your findings?

Dr. Welch: The preoperative diagnosis was intriguing. We followed almost the same line of thinking that Dr. Culver did. We considered as likely diagnoses a right-sided ulcerative colitis, tuberculosis and lymphoma. Of those three we thought that tuberculosis was the most likely, both before and at the time of operation, particularly since the disease was chiefly in the cecum and there were calcified lymph nodes. The outside of the small bowel was entirely normal at the time of operation; the cecum was quite edematous and thickened. The question about the proper type of operation to do arose. I thought establishing a diagnosis was fully as important as curing the subacute obstruction and therefore did a colectomy on the right, with anastomosis of the ileum to the transverse colon.

Dr. Cohen: The entire 24 cm. of lower ileum submitted for examination was indurated and thickened, as was the attached mesentery. A number of large edematous lymph nodes were present in the mesentery. The region of the ileocecal valve was severely involved, and the first several centimeters of cecum were thickened. When the bowel was opened several large ulcerations were found in the ileal mucosa. The remaining mucosa was congested and edematous. Ulcers were present at the ileocecal valve, and the lumen was narrowed. Histologically, these ulcers formed tracts, which penetrated deep into the submucosa and muscularis. The submucosa was edematous and in areas fibrosed. Lymphoid infiltration and follicle formation were prominent. Occasional granulomas were noted in relation to markedly dilated lymphatic channels. All these findings are classic of regional ileitis. The thickened bowel, mesentery and hyperplastic lymph nodes certainly accounted for the right-lower-quadrant mass palpated.

The diagnosis of hypertrophic tuberculous ileitis was a more frequent one before the era of regional ileitis. I think that in reviewing these older cases of hypertrophic ileal tuberculosis one would find that a considerable proportion would fall into the regional-enteritis classification of today. This entity itself is deserving of considerable further investigation and clarification. In this country and in other areas where bovine tuberculous infection is well controlled it is quite unusual to find intestinal tuberculosis in the absence of more generalized infection, particularly of the lungs. No tubercle bacilli were found in this case.

CASE 40442

Presentation of Case

A forty-six-year-old man entered the hospital because of muscular weakness and atrophy.

About eight years before admission, he had noticed the gradual development of weakness and muscular wasting in the hands, associated with rapid, irregular twitchings of the muscles of the shoulders, arms and hands that did not produce movement at the joints. As time passed, the affected muscles became progressively weaker, although he was able to continue his work as a commercial artist. He had also observed, since the onset of the weakness, that sudden or strong movements of the arm or shoulder muscles resulted in a strong, persistent contraction, which failed to relax immediately. At times these spasms were painful, although they usually were not. Occasionally, they occurred in the jaw muscles. Three years before admission, a neurologist found fairly good strength, with minimal wasting in the shoulders, arms and hands. The neck and sternocleidomastoid muscles were considered to be somewhat small, but strong. There was no abnormality of the cranial nerves or the legs. On gripping strongly, he was unable to relax his grasp, but his fingers went into a position of flexion at the metacarpophalangeal joints and extension at the interphalangeal joints for thirty seconds to one minute. Similar persistent contractions could be demonstrated in the deltoid and other arm muscles. The deep reflexes were exaggerated in the arms and at the knees; the abdominal reflexes were active and symmetrical; the plantar reflexes were normal. There were no sensory changes. Quinine, 0.3 gm. three times daily, was prescribed, after which there was great improvement in the muscular spasms. However, the weakness and twitchings became steadily worse. About three months before admission, he had increasing shortness of breath on slight exertion and required two pillows at night. He had otherwise remained in good general health, although he reported a weight loss of about 40 pounds over the previous five years.

At the age of nineteen, during a world epidemic, he had had a two-month illness called "encephalitis" in which he had headache, was drowsy and yet slept poorly, and felt "nervous." He made a complete recovery from this. He had had no other noteworthy illnesses. The family history was unremarkable.

Physical examination showed a generally thin man, who was using the accessory muscles of respiration. The chest expanded poorly, and no movement of the diaphragm could be demonstrated by percussion. Breath sounds were diminished throughout both lungs. The heart was normal. The remainder of the general examination was not remarkable.

On neurologic examination, he was alert, oriented and co-operative. The eyes, including the pupils, and ocular movements were normal. There was no facial weakness. Speech was very slightly nasal, although the palate moved well. There was no weakness or atrophy of the tongue, in which there were no definite fasciculations or fibrillations. The neck, shoulder, scapular and arm muscles were moderately weak, and there was severe weakness and wasting of the small muscles of the hands, especially on the right. The muscles of the legs and feet were fairly strong, although not normally so, with greatest weakness distally. There were widespread, coarse fasciculations in the arms, hands and legs. There was difficulty in immediately relaxing a firm hand grasp, and strong extension of the knee against resistance resulted in mild cramps in the quadriceps muscle. The deep reflexes and abdominal reflexes were present and equal; the plantar reflexes were normal. There were no sensory abnormalities.

The temperature was 99°F., the pulse 64, and the respirations 18. The blood pressure was 130 systolic, 70 diastolic.

Examinations of the blood and urine were negative. Lumbar puncture gave clear cerebrospinal fluid under a pressure equivalent to 80 mm. of water; the fluid, which contained no cells, had a total protein of 19 mg. per 100 cc. and gave a colloidal gold reaction of 0001110000 and a negative Wassermann reaction.

An electromyogram, performed with surface electrodes on the quadriceps, hamstring, anterior-tibial and gastrocnemius muscles bilaterally, disclosed spontaneous fasciculations, but normal activity with voluntary contractions. Similar bilateral recordings from the biceps, triceps and flexor and extensor muscles of the wrist revealed fasciculations, most marked in the right biceps and wrist extensor muscles. Voluntary contraction of the right arm showed a failure of relaxation of all muscles lasting eighteen seconds. The patient was found dead in bed on the morning of the fourth hospital day.

Differential Diagnosis

Dr. John Walton*: This interesting case, like all those discussed in this amphitheater, presents certain inconsistencies and difficulties in diagnosis.

There were three striking clinical features: progressive atrophy of the limb musculature, particularly in the upper limbs and always most severe in the distal part of the extremities; widespread muscular fasciculations; and cramps provoked by movement and associated with difficulty in relaxation of muscles, particularly those controlling the grip. I think it would be as well to consider each of these salient features of the story individually to determine what produced them.

Muscle atrophy was mainly peripheral, was much less severe proximally and in the late stages involved the diaphragm and perhaps the intercostal muscles. Such muscular atrophy could have resulted from disease in the anterior-horn cells, in the spinal anterior nerve roots, in the peripheral nerves or in the muscles themselves. Motor-neuron or motor-system disease, which immediately springs to mind as the probable cause of this clinical picture, is probably a single

*Nuffield Foundation Fellow in Neurology, Massachusetts General Hospital; research assistant, Department of Medicine, Royal Victoria Infirmary, Newcastle upon Tyne, England.

entity although it may be manifested in three distinct clinical forms. The first is the progressive muscle atrophy of Aran and Duchenne; the second and most common is amyotrophic lateral sclerosis, with atrophy of muscles in the upper limbs and spasticity in the lower; and the third is progressive bulbar palsy, in which the atrophy and motor weakness usually begin in muscles supplied by the medulla or bulb. The picture of progressive peripheral muscular wasting with widespread fasciculations in this patient is characteristic of progressive muscular atrophy, but the brisk tendon reflexes in the lower limbs suggest an element of lateral sclerosis. One slight inconsistency is the eight-year history since many patients fail to survive so long. The disease is often fatal within two to six years of the onset. On the other hand Müller,[1] in a recent study of this disease, found that some patients survived for fifteen years so that this certainly does not rule out the diagnosis.

One possible cause of nerve-root disease in such a case is carcinomatosis involving the meninges, with widespread infiltration of anterior roots and spinal nerves, and this may give rise to a progressive peripheral atrophy. The same statement is true of cervical spondylosis (multiple disk degeneration in the cervical spine), which may result in pressure on multiple roots, causing atrophy in the muscles of the upper limbs, and at the same time may compress the spinal cord, giving increased reflexes and sometimes spasticity in the lower limbs. Of course, inflammatory disease of the meninges like meningovascular syphilis may involve nerve roots in the cervical region and also the cord, giving the picture of syphilitic amyotrophy. I think the negative spinal-fluid findings rule out several of these diagnoses, and in fact a number of other points, which I shall discuss in a moment, make any of them unlikely.

Turning now to the peripheral nerves, I wonder if this could have been a polyneuropathy, of which there are multitudinous causes. The absence of sensory loss in this case is very much against the commoner types of polyneuropathy, but, on the other hand, we sometimes see cases of polyneuropathy that are entirely motor and show no sensory changes whatever. There is no doubt that this picture could have been caused by a predominantly motor type of peripheral neuropathy.

Finally, we come to the muscles. A disease of the myoneural junction like myasthenia gravis could not conceivably produce this clinical picture. Could the condition have been a muscular dystrophy or myopathy? The commonly occurring types of muscular dystrophy usually begin in the proximal muscles of the limbs and only in the late stages do they spread to involve the more distal muscles. This, however, is not true of the very rare distal myopathy described by Gowers[2] and, more recently, by Welander[3] in Scandinavia, but in distal myopathy fasciculation of muscles is virtually unknown and certainly is never so gross as that seen in this case. Cases of muscular dystrophy of all types practically never show fasciculations. Another heredofamilial myopathy, myotonic dystrophy or dystrophia myotonica, is characterized by myopathic muscular wasting and weakness in the peripheral muscles of both upper and lower limbs, but this disease is always associated with involvement of the sternocleidomastoid, temporal and masseter muscles, and with myotonia, or difficulty in relaxation of grip. Furthermore, there are usually endocrine disturbances in these patients; the males have frontal baldness and gonadal atrophy. Another characteristic and almost invariable feature of dystrophia myotonica is cataract. Apparently, in the case under discussion, the eyes were normal. Furthermore, in all cases of dystrophia myotonica there is some involvement of facial muscles; in this patient the face was normal. For all these reasons I do not think that this was dystrophia myotonica, although the muscular cramps and the failure to relax the grip were very suggestive of myotonia.

Could this have been thyrotoxic myopathy or some other myopathy of metabolic cause? Apart from the weight loss of 40 pounds in five years, which, although somewhat severe, could have been a result of the muscular wasting, there was no evidence of thyrotoxicosis. Sometimes, the myopathy of thyrotoxicosis precedes the other manifestations by a number of years, but I should think that after eight years there would have been some other manifestations of this disease, and certainly none were mentioned in the protocol. In thyrotoxic myopathy, too, atrophy and weakness of muscles are most often proximal; furthermore, fasciculations are rare, although they have been described. I think I can dismiss polymyositis or dermatomyositis very quickly. This is practically always a disease of the proximal muscles. In some cases there is minimal and in others severe skin involvement; fasciculations are very rare. To me this clinical picture is not at all like that of polymyositis.

Although fasciculation in muscle has been proved to be a phenomenon that arises peripherally, because it persists after blocking or section of the motor nerve, it is undoubtedly true that most patients with widespread fasciculations are proved to have disease of the anterior-horn cells. As I have mentioned already, this phenomenon is seen most clearly and frequently in patients with progressive motor-neuron disease—amyotrophic lateral sclerosis, progressive muscular atrophy and progressive bulbar palsy. However, it is occasionally seen in other conditions that may damage the anterior-horn cells, such as syringomyelia, peripheral neuropathy and cervical-disk disease, but it is not usually so marked and widespread as in this case. Fasciculation in muscles may be benign and widespread and is frequently discovered in medical students and medical practitioners who happen to notice that their muscles are twitching. A diagnosis of myokymia has been applied to this condition of widespread benign fasciculations, in which, however, the fasciculations tend to involve two or three motor units, not a single motor unit, and clinically are much coarser than those in motor-neuron disease. The fact

that I am discussing the case here today is very good evidence that this was not a benign disorder.

Lastly, I shall consider the muscular cramps and the impaired ability to relax the muscles after a strong grip or after a forceful movement. These were powerful, sustained contractions, which were invariably initiated by voluntary movement and did not occur spontaneously; the description was absolutely characteristic of myotonia. As described, these cramps were not those seen in tetany, salt depletion, hypocalcemia or hypoparathyroidism. They were not like the aching, nagging pains resulting from the extrapyramidal rigidity of muscles in Parkinson's disease, nor were they like the sharp cramps and the flexor and extensor spasms that one sees in patients with disease of the pyramidal tracts and spasticity. None of these seem to fit the description that we are given in this case; the only one that would explain the clinical findings is myotonia. I do not think that this was a so-called myotonoid disturbance, the slow lethargic failure to relax muscle usually seen in the large, bulky muscles of patients with Hoffmann's syndrome — in other words in cases of myxedema with muscle involvement. Some patients with myxedema have large, bulky muscles, which tend to be painful and the seat of nagging cramps; relaxation in these muscles is often impaired. Fasciculations would not be expected in Hoffmann's syndrome, and certainly the other findings in this case rule out any suggestion of myxedema. Relief by quinine is also very characteristic of myotonia. Although quinine may often relieve muscular cramps from whatever cause, the relief is usually most striking in patients with myotonia; for this reason I think that I should have to conclude that the phenomenon that this patient showed was true myotonia. Was the failure to relax the grip made worse by cold?

DR. EDWARD P. RICHARDSON, JR.: We do not have sufficient information to answer that question.

DR. WALTON: Did the patient have a test of the basal metabolic rate or recent calcium and phosphorus determinations?

DR. RICHARDSON: No.

DR. WALTON: Before attempting to correlate the muscular atrophy, fasciculations and cramps—this apparently myotonic phenomenon—I shall look briefly at the other findings. There was a previous history of encephalitis, which seems clearly to have been encephalitis lethargica. A number of cases of amyotrophic lateral sclerosis occurring as a sequel to epidemic encephalitis have been reported; however, in most of these there was evidence of Parkinson's disease as well as the manifestations of motor-neuron disease. Furthermore, the latent period is not usually so long. In this case it was twenty-seven years before the muscular atrophy began. This relation was recently discussed very fully by Greenfield and Matthews,[4] who reported 2 cases of amyotrophic lateral sclerosis occurring as a sequel to epidemic encephalitis but both patients had postencephalitic Parkinson's disease; they referred to other cases in the literature in which there had been no evidence of Parkinson's disease but simply the picture of amyotrophic lateral sclerosis, apparently as a sequel to encephalitis.

The investigations in this case were never of any great help. The cerebrospinal-fluid examination excluded any of the more active forms of polyneuropathy, in which the protein is usually raised, and the electromyogram simply confirmed the presence of fasciculations. Will you tell us about the electromyogram, Dr. Schwab?

DR. ROBERT S. SCHWAB: The examination showed numerous fasciculations, some large, some small and some series of identical-sized ones. Throughout the record there were continual discharges of this type in the legs and arms. These examinations were all done on the ink writer by surface electrode, and I cannot find any evidence that cathode-ray studies were done. When the patient contracted the flexor muscles of the wrist and then was told to relax, he was unable to do so; the contractions continued for eighteen seconds and then began to disappear. This is the myotonia response.

DR. WALTON: It is unfortunate that a needle electrode study was not done because in such a patient one might expect to find not only spontaneous fasciculations but also spontaneous fibrillation or spontaneous contraction of single muscle fibers as distinct from motor units, a phenomenon that is probably seen only in denervated muscle. It would also have been interesting because a needle electrode study in cases of true myotonia shows a characteristic myotonic discharge—chains of oscillations of high potential waning slowly and giving a characteristic sound in the loud speaker rather like that of a dive bomber.

Finally, I must try to correlate the different findings in this case. The great difficulty is to reconcile on the one hand muscular atrophy and fasciculations, which are characteristic of motor-neuron disease, particularly when associated with increased reflexes in the lower limbs, and on the other hand the muscle cramps and delayed relaxation, which are very suggestive of myotonia and for which I can think of no other explanation. Classic myotonia occurs only under two circumstances, in myotonia congenita (Thomsen's disease) and in dystrophia myotonica. In patients with myotonia congenita this phenomenon is usually present from birth, affects all voluntary muscles, is made worse by cold and is relieved after the patient has moved about for a while. These cases run an essentially benign course. I cannot believe that this patient had myotonia congenita that did not appear until the age of forty-six. Dystrophia myotonica may be excluded for reasons already given.

A condition of myotonia of acute onset in adult life was described first by Talma[5] in 1892 and called myotonia acquisita. Thomasen,[6] who recently wrote a monograph on myotonia, has discussed this condition in great detail and has come to the conclusion that all Talma's patients were suffering from myotonia congenita, dystrophia myotonica or Hoffmann's syndrome—namely, myxedema, with muscle involvement. Many people now believe that myotonia ac-

quisita is not a distinct entity. Hence I do not believe that this was a case of myotonia acquisita, and as I have already mentioned the clinical picture was not like that of polyneuritis or thyrotoxic myopathy.

My conclusion must be that this was an example of progressive motor-neuron disease, probably of the type of amyotrophic lateral sclerosis, in which symptomatic myotonia occurred. Recently, there has been a report by Worster-Drought and Sargent[7] of reactive myotonia in cases of polyneuritis; Worster-Drought mentioned in that paper that he had seen active myotonia in a patient with Charcot–Marie–Tooth disease or peroneal muscular atrophy. The authors' explanation for this phenomenon was that the muscles in a state of partial denervation became hyperirritable and so gave rise to the phenomenon of myotonia; this does, however, seem to be a very facile explanation. I shall nevertheless have to conclude that a similar symptomatic or reactive myotonia occurred in this case.

DR. BENJAMIN CASTLEMAN: Dr. Fisher, would you like to comment on this case?

DR. C. MILLER FISHER: One clinical point that was not touched upon is that the patient was found dead in bed, and I wonder if Dr. Walton would like to comment on that.

DR. WALTON: I did not comment on that because I had taken so much time. The diaphragm was involved, and I believe that he probably had hypostatic pneumonia. I cannot give any other explanation. The sudden death could have been cardiac, but I cannot think that it was related to the muscle disease except so far as he had severe involvement of the muscles of respiration and presumably some degree of respiratory failure.

CLINICAL DIAGNOSES

Bulbar palsy.
Dystrophia myotonica.

DR. JOHN WALTON'S DIAGNOSIS

Amyotrophic lateral sclerosis, with symptomatic myotonia.

ANATOMICAL DIAGNOSIS

Progressive muscular atrophy.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Autopsy did show an acute tracheobronchitis with a great deal of pulmonary congestion; that is all we found as a cause of death. I shall ask Dr. Richardson to discuss the central-nervous-system findings.

DR. RICHARDSON: Dr. Walton has given us an illuminating discussion of the various clinical phenomena that occurred in this case and of the diagnostic possibilities. He was puzzled by the occurrence of classic myotonia in what was otherwise a case of progressive muscular atrophy. This feature also stood out prominently in the minds of the clinicians who saw the patient during life. On pathological examination we found that this was a case of motor-neuron degeneration entirely consistent with the chronic, progressive disease of the motor system that Dr. Walton has discussed. The disease appeared to affect principally the anterior-horn cells of the spinal cord, with minimal involvement of the cranial-nerve motor nuclei. Myelin stains of the cord failed to demonstrate any involvement of the lateral corticospinal tracts, so that perhaps the exaggerated tendon reflexes that were described in the first examination were not significantly exaggerated. Cell stains showed widespread disappearance of anterior-horn cells at all levels in the spinal cord, and most of the few that remained appeared diseased—in that they were pale, or dark and shrunken. There were typical reactive changes in the astrocytes and microglia in the affected regions. As could have been expected there was secondary degeneration in the anterior roots. All these phenomena indicate a chronic destructive process. Parts of the cord other than those specifically affected were intact, and there were no significant changes elsewhere in the nervous system. Representative sections of skeletal muscles demonstrated findings typical of denervation atrophy, with groups of small muscle fibers, corresponding to diseased motor units, interspersed among groups of fibers of normal size, of which the motor-nerve supply had not been affected. This case must be classified as progressive muscular atrophy rather than amyotrophic lateral sclerosis, because of lack of pyramidal-tract involvement.

A PHYSICIAN: Do Thomsen's disease and other diseases in which there is myotonia show anything in the muscles?

DR. RICHARDSON: Thomsen's disease (myotonia congenita) shows nothing that can be recognized as histologically abnormal in the muscle other than some distortion of fibers that may be artifacts due to the abnormal contractility. The muscles in cases of dystrophia myotonica show changes very closely resembling those of progressive muscular dystrophy, which are different from what we find in cases such as this.

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TETRACYCLINE ANTIBIOTICS

A large amount of basic clinical and laboratory information concerning the new antibiotic tetracycline was presented at the Antibiotic Symposium in Washington in October, 1953. Although most of the clinical observations indicated similar activity of tetracycline and its two closely related analogues, chlortetracycline and oxytetracycline, there were appreciable differences in the activity of the agents against some species of bacteria in vitro and against various experimental infections in laboratory animals. Moreover, the clinical data presented then, and others since that time, have been inadequate for reliable comparisons of the efficacy of the three analogues.

In a recent editorial comment[1] Dr. Henry Welch, director of the Division of Antibiotics of the Food and Drug Administration, called attention to the fact that several investigators, in tabulating the comparative sensitivity of various strains of certain species of bacteria, noted severalfold differences in the concentration of one or another of the tetracyclines that were required to inhibit the same strain. He believed that this in itself argued in favor of caution in assigning "equivalent antibacterial activity" to the three tetracyclines. He also observed that a number of clinical reports demonstrated differences in the therapeutic results obtained with these three antibiotics. "Our appraisal of the new antibiotic tetracycline," Dr. Welch argued, "should therefore start with the presumption that it is a new broad-spectrum antibiotic that will face the problems and vicissitudes that will always confront a new drug. . . ."

More recently, Welch and his co-workers[2] reported a study of 338 strains of *Staphylococcus aureus* with distinctive and significant differences in sensitivity to chlortetracycline, oxytetracycline and tetracycline in vitro. Of these three analogues, chlortetracycline appeared to be considerably more active than the other two against this group of staphylococcal strains; tetracycline was only slightly less active, but oxytetracycline was definitely the least active of the three. The difference between chlortetracycline and oxytetracycline had previously been demonstrated in a study of 500 strains of *Staph. aureus* isolated at the Boston City Hospital,[3] among which about a fourth of those that were sensitive to chlortetracycline were either moderately or highly resistant to oxytetracycline; more than two thirds of those that were moderately resistant to the former were highly resistant to the latter, whereas almost all the strains that were resistant to chlortetracycline were equally resistant or more so to oxytetracycline.

Other differences have been noted by workers at the Thorndike Memorial Laboratory.[4,5] Strains of *Proteus mirabilis*, for example, were found to be similarly resistant to chlortetracycline and tetracycline but only moderately resistant to oxytetracycline. On the other hand most strains of other species of proteus — namely, *P. vulgaris*, *P. morganii* and *P. rettgeri*

— appeared to be equally sensitive to all three of the tetracycline analogues.[4] Differences were also reported by these workers in the effects of the three tetracyclines on recently isolated strains of pseudomonas; in this instance oxytetracycline appeared to be the most active, chlortetracycline the least active, and tetracycline intermediate in its activity.[5]

These in vitro findings lend support to Welch's argument for considering chlortetracycline, oxytetracycline and tetracycline as three distinct antibiotics. The data on the development of crossresistance resulting from repeated exposures to any one of the three tetracycline antibiotics in vitro might imply a contrary view.[6] However, actual tests of the sensitivity of strains obtained from patients under treatment with any one of them do not indicate similar degrees of resistance to all three tetracycline analogues. This fact and the differences in the clinical toxicity of the three antibiotics[7] lend additional weight to their individuality as therapeutic agents.

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HELP FOR THE CHRONICALLY ILL

The Massachusetts Department of Public Health has already outlined in these pages the capabilities and purposes of the recently opened Lemuel Shattuck Hospital for the chronically but not hopelessly ill, and there is little doubt that Boston's famous bookseller would approve of the design. With an ultimate bed capacity for 600 patients the hospital will provide the most modern facilities for the study and treatment—not simply the care—of residents of the Commonwealth suffering from chronic diseases and cancer *who may potentially benefit from such hospitalization.*

The hospital, in treating these types of patients according to the most approved methods, will serve also as a teaching center for chronic disease, in affiliation with the three medical schools of Boston and the Harvard School of Public Health; it will have a resident training program, a school for practical nurses and affiliations with schools of physical medicine, occupational therapy and social service. Of equal importance with these functions of investigation and amelioration of chronic disease will be a continuing rehabilitation service, as complete as the circumstances of the disability will permit.

The program is an ambitious one, but it is in keeping with the social and spiritual progress that mankind constantly essays, onward and upward—it may be hoped, forever. Under the direction of the Massachusetts Department of Public Health with its record of honest and capable achievement there is no question that the new hospital will discharge these new functions in the most appropriate manner. A continuing problem of its directors will be to maintain an active turnover of patients to prevent it from becoming a "chronic" hospital in the old meaning of the term.

Some concern has been expressed — as is invariably the case when any new program in public health is projected — whether the new hospital may not be found in competition with the private hospital and the practicing physician. The belief is that the hospital will rather serve a large group of patients for whose study and care there have hitherto been no suitable facilities. It may be expected that the new institution, like the Pondville Hospital, will aid the physician in the care of the type of patients accepted rather than compete with him for their patronage.

FOUR PILLARS OF WISDOM

In reference to the so-called "Vanishing American," recently discussed in these columns, stubborn resistance all along the line to prevent any further reduction in the general practitioner's numbers seems to have developed, despite published figures that appeared to indicate the continued recession of medicine's man of all work. Like the Cheshire cat he recedes and reappears; unlike the outcome of that celebrated animal's periodic fadeouts it is likely that his end stage will be one of increased rather than of lessened prominence. In the correspondence on this subject presented in the issue of October 28 Mr. Funk, a medical student, emphasized the failure of many medical schools to give any encouragement whatsoever to the idea of general medicine, and Captain Haubrich stressed the necessity of general-practice preceptorships to hold students to this ideal of medical service.

A number of schools the country over have established such preceptorships with the good effect noted by Captain Haubrich, and at long last the Harvard Medical School, not particularly conspicuous in recent years as an assembly line for family physicians, has launched a study with the object of integrating the teaching of comprehensive medical care with its school curriculum. This study, financed by a five-year grant of $275,000 from the Rockefeller Foundation, will be developed in and from the Massachusetts General Hospital and will benefit from the experience of the child-care program that has already been conducted for some time in the Children's Medical Service of that hospital, under the patronage of the Hyams Fund.

It would be jumping to conclusions, however, to

identify the new study too closely with the establishment of preceptorships in the ordinary sense of the term. This will not be a matter simply of exposing fourth-year students to the practical aspects of general medicine under the tutelage of physicians who are practicing it successfully. It will be rather a scientific study of the total health needs of individuals as related to families in the vicinity of and receiving medical care from the Massachusetts General Hospital and associated community agencies.

The general purpose of the study as announced last August will be to develop methods for the instruction of students in complete medical care. The program will be directed toward a comprehension of four special pillars of wisdom—normal child growth and development, the early recognition and evolution of chronic disease, hereditary and environmental influences on health and illness, and methods of disease prevention.

The project, therefore, goes beyond the mere establishment of preceptorships, valuable as they are. By integrating the essential aspects of medical care it will bring into the foreground the social and economic obligations of the physician and perhaps lead toward the development of a new and better type of personal medical service and guidance.

LO, THE POOR INDIAN!

A FURTHER indication that where there is smoke there may be some fire emanates from the director of the Federal Trade Commission's recently established Bureau of Consultation, Charles E. Grandey, who, according to a news release, has asked the manufacturers of cigarettes to consider abandoning references to health in their advertising "and to limit cigarette sales appeals generally to quality, taste, flavor and enjoyment."

If this sound advice—which may have nearly the force of a directive—is heeded, gone as with the wind will be even a reference to that elusive cough that cannot be found in a carload; gone will be anything more than the most remote allusion to the various filters that, health-preserving as they can be in other respects, certainly have no apparent bearing on the prevalent belief that tobacco smoke may be a carcinogenic agent.

As an incentive to the abandonment of the health motif by the tobacconists, Mr. Grandey invokes the "spirit in which the industry has entered into the effort to resolve the scientific questions currently presented." He believes—and time, it is hoped, will justify his belief—that the manufacturers will consider this "an especially propitious time to effect voluntary cessation of every questionable claim and implication in their advertising."

As Pope might have written, "Lo, the poor [cigar store] Indian! whose untutor'd mind," and so forth.

Cases of smallpox seem to be greatly on the increase in different parts of New Hampshire, Maine and Vt., notwithstanding there is a sovereign antidote, vaccination.

Boston M. & S. J., *Nov. 8, 1854*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

AREY — Jean G. Arey, M.D., of Gardner, died on August 13. She was in her sixty-second year.

Dr. Arey received her degree from Tufts College Medical School in 1914. She was a member of the staff of Heywood Hospital.

She is survived by her husband, three daughters, two sons, her mother, a sister and two brothers.

FORD — John Francis Ford, M.D., of Roslindale, died on October 9. He was in his eighty-fourth year.

Dr. Ford received his degree from Dartmouth Medical School in 1892.

He is survived by his widow, a daughter and two grandchildren.

PAGE — George T. Page, M.D., of Brookline, died on October 7. He was in his eighty-sixth year.

Dr. Page received his degree from Harvard Medical School in 1896.

He is survived by his widow.

PAUL — Luther G. Paul, M.D., of Newton Center, died on October 6. He was in his eighty-fourth year.

Dr. Paul received his degree from Harvard Medical School in 1899. He was a fellow of the American College of Surgeons and a member of the Boylston Medical Society and the staff of the Carney Hospital.

He is survived by his widow, two daughters and a brother.

SIMONS — Sidney M. Simons, M.D., of Arlington, died on October 8. He was in his fifty-fifth year.

Dr. Simons received his degree from Tufts College Medical School in 1924. He was chief anesthetist at Symmes Arlington Hospital, a member of the staff of the Boston City Hospital and a fellow of the American Medical Association.

He is survived by his widow, his mother and two brothers.

CORRESPONDENCE

MEETING OF MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

To the Editor: At a meeting of the Middlesex South District Medical Society held on September 30 the following material and the resolution, which was passed by unanimous vote, were accepted with such enthusiasm by the members present that it is considered to be of general interest:

The program of the American Academy of General Practice is for the following purposes:

1. Post-graduate courses for the general practitioner.
2. Establishment of general Practice Departments in hospitals. The American Medical Association, the American College of Surgeons, and the Accreditation Boards approve of the above program.

In view of this backing, I would like Middlesex South also to approve this program. The American Academy of General Practice, whose membership at present is around 18,000 (eighteen thousand), by its work has been able to establish departments of General Practice in almost half the hospitals in the United States. There are 150,000 general practitioners in the United States. Since Middlesex South has a membership of about a thousand, it is obvious that a large majority are general practitioners. It is also a well known fact that all the hospitals in Middlesex South have no department of general practice as part of its functioning staff.

It is my aim, by the motion I am going to make, to put Middlesex South on record as being in favor of establishing such departments in the interests of the general practitioner in the hospitals of the Middlesex area.

Therefore, I move that the Chair appoint a committee to advance the establishment of general practice departments as part of the staff organization in the hospitals of Middlesex South, and to report on their progress at the earliest subsequent meeting.

S. Edward Chalfin, M.D.

Alexander A. Levi, M.D., *President*
Middlesex South District Medical Society

Boston

REGARDING MYASTHENIA GRAVIS

To the Editor: The Medical Progress report on myasthenia gravis by Dr. Henry R. Viets, which appeared in the July 15 issue of the *Journal*, refers to the belief recently expressed by Ravin et al., in their study entitled "Histochemical Localization of Acetylcholinesterase in Nervous Tissue" (*J. Pharmacol. & Exper. Therap.* **107**:37-53, 1953), that the histochemical method in 1950 described by me in an article on the subject "The Histochemical Differentiation of Types of Cholinesterases and Their Localization in the Tissues of the Cat" (*J. Pharmacol. & Exper. Therap.* **100**:158-179, 1950) leads to erroneous localization of specific (true, acetyl-) cholinesterase. This is undoubtedly correct, as I pointed out in 1951 in my report, "The Elimination of Enzymatic Diffusion Artifacts in the Histochemical Localization of Cholinesterases and a Survey of Their Cellular Distributions" (*J. Pharmacol. & Exper. Therap.* **103**:153-171, 1951), which described a modification, developed on the basis of quantitative studies, to eliminate enzymatic diffusion on artifacts. Regarding other possible sources of error there is no evidence of lack of penetration by the positively charged acetylthiocholine molecule in fresh frozen sections, or of artifactitious adsorption of the reaction product to negatively charged portions of the cell. Thus, with the modified method, neuronal membranes and cytoplasm are stained for cholinesterase activity whereas nuclei remain unstained. The precision of the modified procedure has been confirmed by Couteaux and Taxi, in their study entitled "Recherches histochimiques sur la distribution des activités cholinestérasiques au niveau de la synapse myoneurale" (*Arch. d'anat. microscop. et de morph. expér.* **41**:352-392, 1952), by Pearse, in his book, *Histochemistry, Theoretical and Applied* (Boston: Little, Brown, 1953), and by Denz, in his report, "On the Histochemistry of the Myoneural Junction" (*Brit. J. Exper. Path.* **34**:329-339, 1953), the last named having employed the technic in preparing photomicrographs of motor end plates shown in the paper cited.

I trust that you will consider the clarification of this point of sufficient importance to call it to the attention of your readers.

George B. Koelle, M.D.

Philadelphia

BOOK REVIEWS

The Insight Test: A verbal projective test for personality study. By Helen D. Sargent, Ph.D. With a foreword by Pearl G. Knapp, Ph.D. 8°, cloth, 276 pp., with illustrations. New York: Grune and Stratton, 1953. $6.75. (*Menninger Clinic Monograph Series* No. 10.)

The author presents a manual for her unique paper-and-pencil projective test, which she first reported in 1944. The book is composed of two parts: the manual proper; and illustrative protocols from 7 clinical groups. Subjects in this test respond to a number of conflict situations that are scored for expressed affect (A), defense (D) and malignancy (M). There are a number of subscorings within these categories. The author makes much of the A/D ratio. She presents an interesting personality theory, on which the test is based.

Although she advances some statistical data in support of the test, these fall short of quantitative proof. Qualitatively, the test may furnish clinical leads to psychopathology, but in this respect it merely offers areas to be speculated on rather than areas that are given substantiation.

Hermann O. Schmidt, Ph.D.

Science and Man's Behavior: The contribution of phylobiology. By Trigant Burrow, M.D., Ph.D. Edited by William E. Galt, Ph.D. Including the complete text of *The Neurosis of Man.* 8°, cloth, 564 pp., with 9 tables and 26 illustrations. New York: Philosophical Library. $6.00.

For many years Dr. Burrow worked intensively in a field of his own, studying people as he saw them and documenting and reporting his results. He was a highly original person and even used words with his own special meaning. This large volume contains his objective and subjective interpretation of many years' work, focused on man and man's behavior.

Now that he has written his last it has remained to his co-workers to assemble and organize his various contributions. Dr. Galt, long associated with Dr. Burrow, has performed this task conscientiously and thoroughly in this interesting volume. It is not light reading, but in many parts it is extremely provocative and stimulating. It mirrors the view of psychiatry that Dr. Burrow watched over a long period, framed permanently in this substantial edition. This is a book for scholars and students of the science of man's behavior.

Merrill Moore, M.D.

NOTICES

NEW ENGLAND CARDIOVASCULAR SOCIETY

The next meeting of the New England Cardiovascular Society will be presented by the Boston City and Massachusetts General hospitals in Morse Auditorium, Museum of Science, Science Park, Boston, November 15 at 8 p.m.

The program is as follows:

Boston City Hospital. Dr. Laurence B. Ellis, presiding.

Collateral Circulation in Cerebral Lesions. Dr. Derek Denny-Brown.

Methods and Concepts Pertaining to Prothrombopenic Anticoagulants. Dr. Herbert S. Sise.

Changes in the Systemic Circulation in Hepatic Disease. Dr. Walter H. Abelmann.

Massachusetts General Hospital. Dr. Edward F. Bland, presiding.

Arterial Grafting for Arteriosclerotic Obliterative Disease. Dr. Robert S. Shaw.

Comparison of Pulmonary Arteriolar Resistance and Pulmonary Vascular Pathology in Patients with Mitral Stenosis. Drs. Fairfield Goodale, Jr., Guillermo Sanchez, Allan L. Friedlich, J. Gordon Scannell and Gordon S. Myers.

Clinical and Experimental Observations on Respiration and Circulation after Bilateral Glossopharyngeal-Nerve Section. Drs. James H. Currens, Thomas Ballantine, John Drew and Mandel Cohen.

Physicians and medical students are invited.

NU SIGMA NU

A lecture sponsored by Nu Sigma Nu will be given on Thursday, November 18, at 5:00 p.m. in the auditorium of the Jimmy Fund Building, Children's Medical Center.

Dr. Thomas Hale Ham, professor of medicine, Western Reserve University School of Medicine, will speak on the topic "A Progress Report on an Experiment in Medical Education."

SOUTH END MEDICAL CLUB

A meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, on November 16 at 12 noon. Dr. David Ayman will speak on the subject "Myocardial Infarction." All physicians are invited.

INDUSTRIAL MEDICINE SYMPOSIUM

A symposium on "Industrial Medicine for the General Practitioner," sponsored by the Committee on Industrial Health of the Massachusetts Medical Society will be held at the Sheraton Plaza Hotel, Boston, on November 17, from 9:30 a.m. to 4:00 p.m.

The program is as follows:

Introduction. Dr. George Wilkins.

The Complexities of the Workmen's Compensation Act Translated for the General Practitioner. Timothy H. Donohue.

Rehabilitation: Who, what, when and where. Dr. William F. Hickey, Jr.

Where Is Industrial Medicine Going? Dr. R. B. O'Connor.

Anticipating Senescence. Dr. Edward J. Steiglitz.

Film: What Happens, in Industry, to the Family Physician's Note?

Part-Time Work in Industry. Dr. Robert Putnam.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION

The next examinations for the American Board of Physical Medicine and Rehabilitation will be held in Philadelphia, June 5 and 6, 1955. The final date for filing applications is March 1. Applications for eligibility for the examinations should be mailed to the secretary, Dr. Earl C. Elkins, 30 North Michigan Avenue, Chicago 2, Illinois.

GROSS PRIZE OF THE PHILADELPHIA ACADEMY OF SURGERY

Essays will be received in competition for the Samuel D. Gross Prize ($1500) of the Philadelphia Academy of Surgery until July 15, 1955. Articles should not exceed 150 printed pages (octavo) and should be illustrative of some subject in surgical pathology or surgical practice, based on original investigations, written by single authors who are American citizens, typewritten in English, distinguished by a motto and accompanied by a sealed envelope bearing the same motto and containing the name and address of the writer, and submitted to the Trustees of the Samuel D. Gross Prize of the Philadelphia Academy of Surgery, care of the American College of Physicians, 19 S. 22d Street, Philadelphia, Pennsylvania.

SOCIETY MEETINGS AND CONFERENCES

November, 1954–April, 1955. Postgraduate Medical Institute. Page 451, issue of September 9.

November, 1954–May, 1955. Sanitary Engineering Center Training Programs. Page 122, issue of July 15.

November 2–6. National Society for Crippled Children and Adults. Page 631, issue of October 7.

November 5 and 6. Nutrition Conference. Page 758, issue of October 28.

November 6. Massachusetts Hospital School Symposium. Page 495, issue of September 16.

November 6, 1954–May 7, 1955. Middlesex South District Medical Society. Postgraduate Course. Page 758, issue of October 28.

November 11. Symposium on Chronic Pulmonary Disease. Page 721, issue of October 21.

November 11–13. American College of Cardiology. Page 722, issue of October 21.

November 12. Memorial Center for Cancer and Allied Diseases Conference. Page 544, issue of September 23.

November 12 and 13. Inter-Society Cytology Council. Page 968, issue of June 3.

November 12–24. Consultation Clinics for Crippled Children in Massachusetts. Page 721, issue of October 21.

November 15. New England Cardiovascular Society. Page 793.

November 15–19. American College of Surgeons. Page 496, issue of September 16.

November 15–26. Laboratory Diagnosis of Tuberculosis Course. Page 246, issue of August 5.

November 15, 1954–January 17, 1955. Hartford Medical Society. Page 496, issue of September 16.

November 16. Harvard Medical Society. Amphitheater E, Department of Pharmacology, Harvard Medical School.

November 16. South End Medical Club. Notice above.

November 16 and 17. New England Diabetes Fair. Page 721, issue of October 21.

November 17. American Trudeau Society. Page 588, issue of September 30.

November 17. Massachusetts Academy of General Practice. Page 721, issue of October 21.

November 17. Industrial Medicine Symposium. Notice above.

November 18. Nu Sigma Nu. Page 793.

November 29–December 1. Association of Military Surgeons of the United States. Page 631, issue of October 7.

December 1, February 4 and April 8. Massachusetts Society for Research in Psychiatry. Page 679, issue of October 14.

December 3, 1954; February 4 and April 1, 1955. New England Society of Anesthesiologists. Page 1054, issue of June 17.

December 5. American Academy of Dental Medicine. Page 1092, issue of June 24.

December 7. Medical Television Program. The Doctor. (Cavalcade of America.) Page 631, issue of October 7.

December 8. New England Pediatric Society. Page 968, issue of June 3.

December 8. Postgraduate Seminar in Psychiatry and Neurology. Page 452, issue of September 9.

December 8 and 9. Myasthenia Gravis Foundation Conference. 2 East 103d Street, New York.

December 13–17. Congress of Obstetrics and Gynecology. Page 748, issue of April 29.

January 3–May 9, 1955. Postgraduate Seminar in Psychiatry and Neurology. Page 452, issue of September 9.

January 10–15. Course in Care of Atomic Casualties. Page 285, issue of August 12.

February 7–9. McIntyre-Saranac Conference. Page 410, issue of September 2.

February 11–25. Pan-American Academy of General Practice. Page 496, issue of September 16.

March 7–12. Course in Care of Atomic Casualties. Page 285, issue of August 12.

May 4 and 5. American Psychosomatic Society. Page 286, issue of August 12.

June 5 and 6. American Board of Physical Medicine and Rehabilitation. Notice above.

June 21–25. National Association for the Prevention of Tuberculosis. Page 540, issue of March 25.

Calendar for the Week Beginning Thursday, November 11

Thursday, November 11
Holiday

Friday, November 12
Second Annual Inter-Society Cytology Council. Hotel Statler, Boston.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–1:00 p.m. Medical Grand Rounds. Dr. Proger and Staff. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*4:00–5:00 p.m. Child Psychiatry. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Waltham Street.
*4:00–6:00 p.m. X-Ray Conference. Dr. Merrill Sosman. Stearns Auditorium, New England Center Hospital.

Saturday, November 13
Second Annual Inter-Society Cytology Council. Hotel Statler, Boston.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Anesthesia Conference. Dr. Etsten. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*9:00–10:30 a.m. Surgical Grand Rounds. Dr. Child and Staff. Stearns Auditorium, New England Center Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*10:30 a.m.–12:00 m. Surgical History Meeting. Stearns Auditorium, New England Center Hospital.
*11:00 a.m.–12:00 m. Hematology Clinic. Dr. William Dameshek. Pratt Lecture Hall Joseph H. Pratt Diagnostic Hospital.

Monday, November 15
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. New England Deaconess Hospital.
*8:30–9:30 a.m. Clinic by Entire Surgical Staff and Anesthesia Staff. Cheever Amphitheater, Dowling Building. Boston City Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m.–1:00 p.m. Metabolism Conference. Dr. Schwartz. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Pediatric Medical Surgical Rounds. Drs. Baty and Swenson. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.

(Concluded on page xxiii)

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1. Garrett, T. A.: Personal communication.

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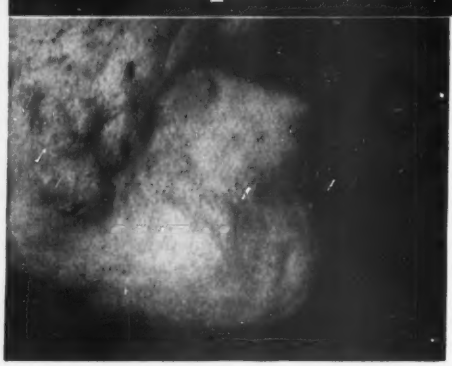

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*Lucia, S. P.: Wine as Food and Medicine, New York, The Blakiston Company, Inc., 1954.

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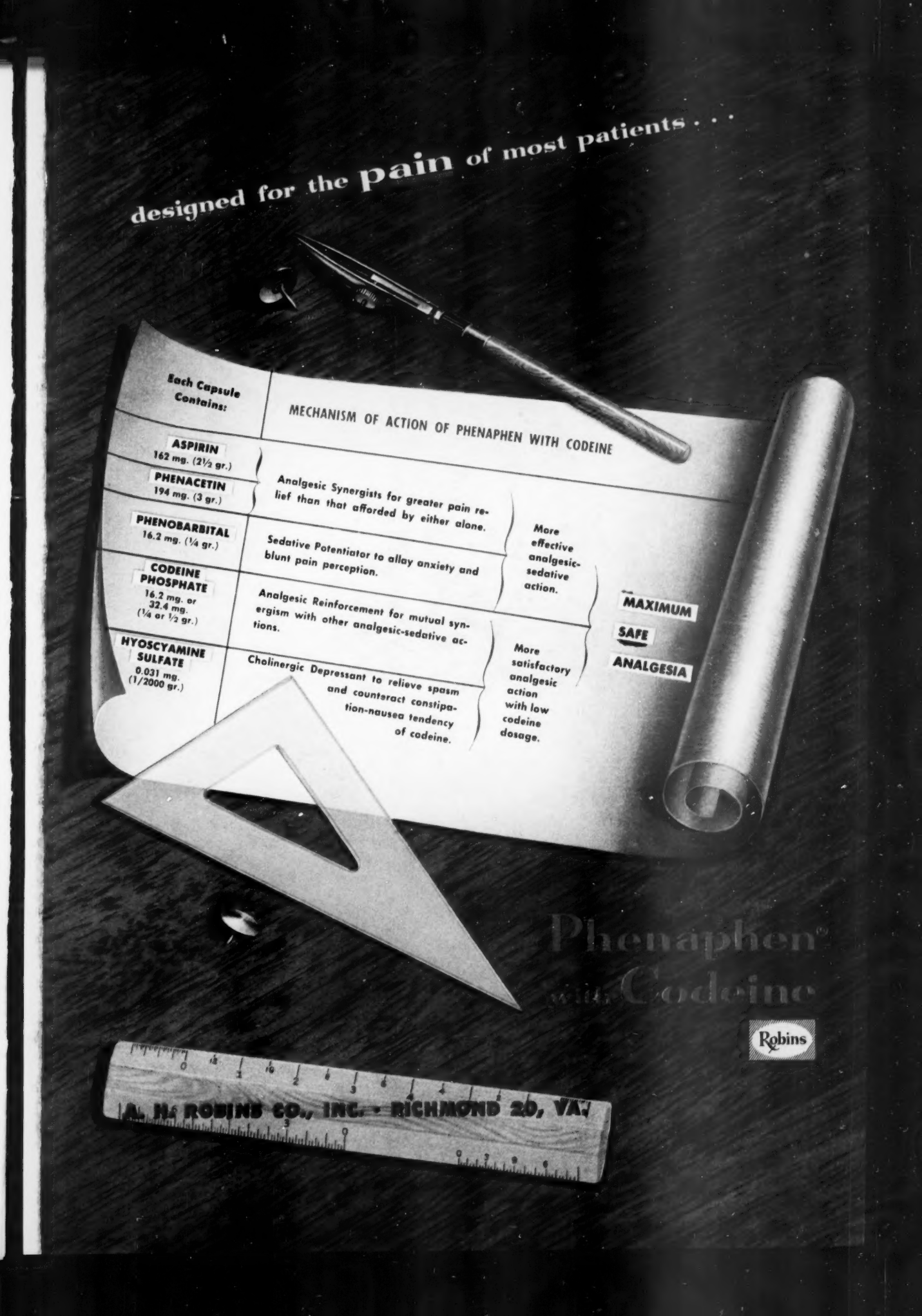
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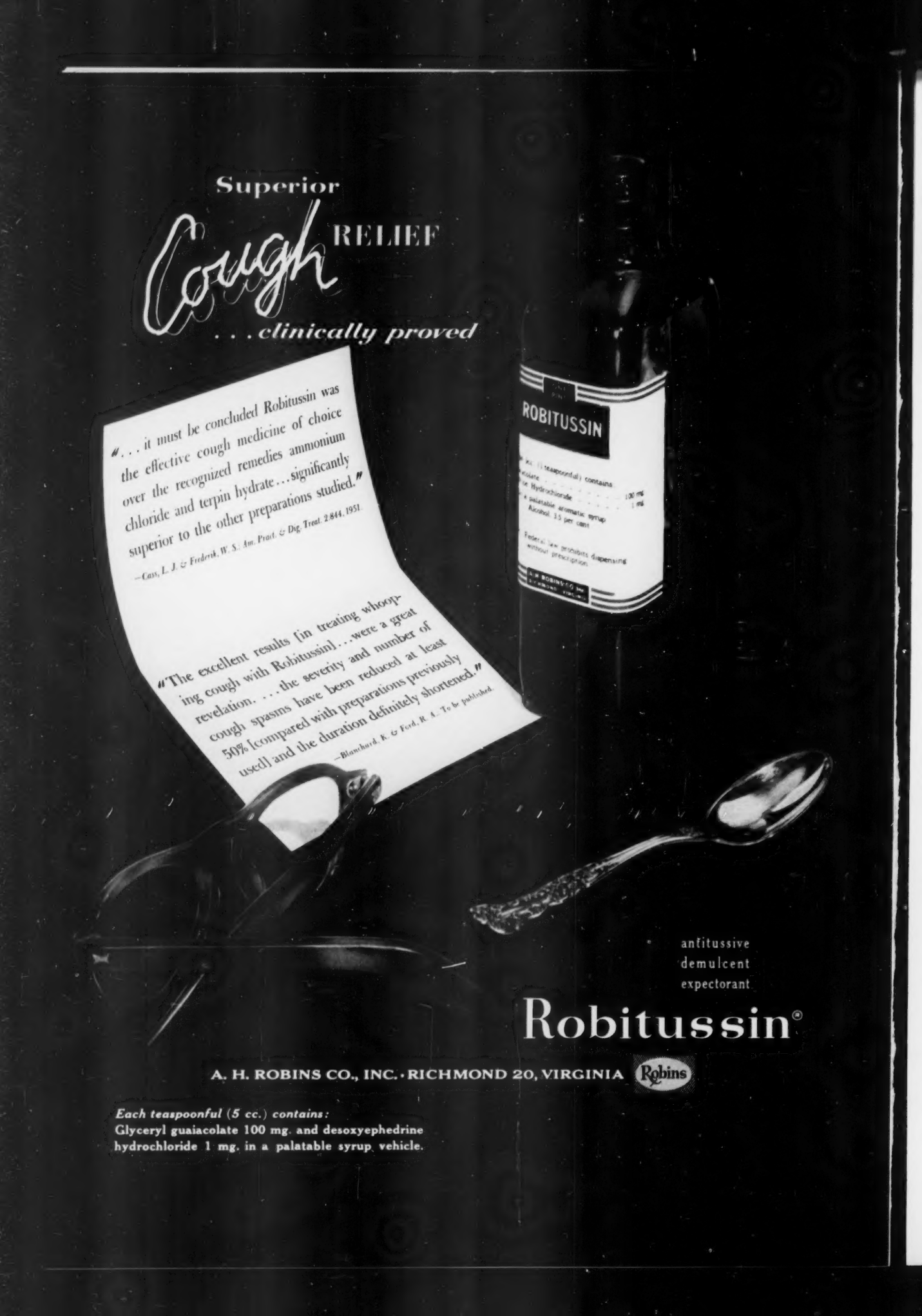

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1. Rath, C. E.: M. Clin. North America 34: 1779, 1950.

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(Concluded from page 794)

*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*4:00 p.m. Clinicopathological Conference. Pathology Conference Room, Beth Israel Hospital.
*4:00–5:00 p.m. Surgical Pathology. Dr. MacMahon. Stearns Auditorium, New England Center Hospital.
*5:00–6:30 p.m. Anesthesia Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00 p.m. New England Cardiovascular Society. Morse Auditorium, Museum of Science, Science Park, Boston.
*8:30 p.m. Hartford Medical Society. Cardiac Arrhythmias: Mechanisms and method of treatment. Dr. Harry Gold. Hunt Memorial Building, Hartford.

TUESDAY, NOVEMBER 16
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:00 a.m. Geriatrics Clinic. Peter Bent Brigham Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m. Pediatric Grand Rounds. Cheever Amphitheater, Dowling Building, Boston City Hospital.
*12:00 m. South End Medical Club. Boston Tuberculosis Association, 554 Columbus Avenue, Boston.
*12:00 m.–1:00 p.m. Pediatric Combined Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
12:30–1:30 p.m. Medical Journal Club. Joslin Clinic. New England Deaconess Hospital.
*4:00–5:30 p.m. Anesthesia Conference. Dr. Etsten. Stearns Auditorium, New England Center Hospital.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting Followed by Clinical Conference (Medical, Surgical, Obstetrical). Faulkner Hospital.
*8:00 p.m. Combined Rounds. Children's Hospital.
8:15 p.m. Harvard Medical Society. Amphitheater E, Department of Pharmacology, Harvard Medical School.

WEDNESDAY, NOVEMBER 17
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30 a.m.–4:00 p.m. Industrial Medicine Symposium. Sheraton Plaza Hotel, Boston.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by a Member of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m. Orthopedic Grand Rounds. Bigelow Amphitheater, White 3A, Massachusetts General Hospital.
*11:00 a.m. Boston State Hospital Psychiatry Seminar. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Clinicopathological Conference. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:00 m.–1:00 p.m. Roentgen Diagnostic Conference. 5th floor teaching unit, Beth Israel Hospital.
*12:30 p.m. Weekly Pathological Meeting. Joslin Auditorium, New England Deaconess Hospital.
*12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*1:00 p.m. Massachusetts General Hospital Hand Clinic. Out-Patient Department.
*2:00 p.m. Rectal Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
*4:00–6:00 p.m. Overholt Thoracic Conference. Joslin Auditorium, New England Deaconess Hospital.
*6:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*7:00–9:00 p.m. Postgraduate Seminar in Pediatric Neurology and Psychiatry. Psychosomatic Disorders. Dr. Dane G. Prugh. Walter E. Fernald State School, Waltham.
*7:30–9:30 p.m. Lahey Clinic Lecture. Joslin Auditorium, New England Deaconess Hospital.

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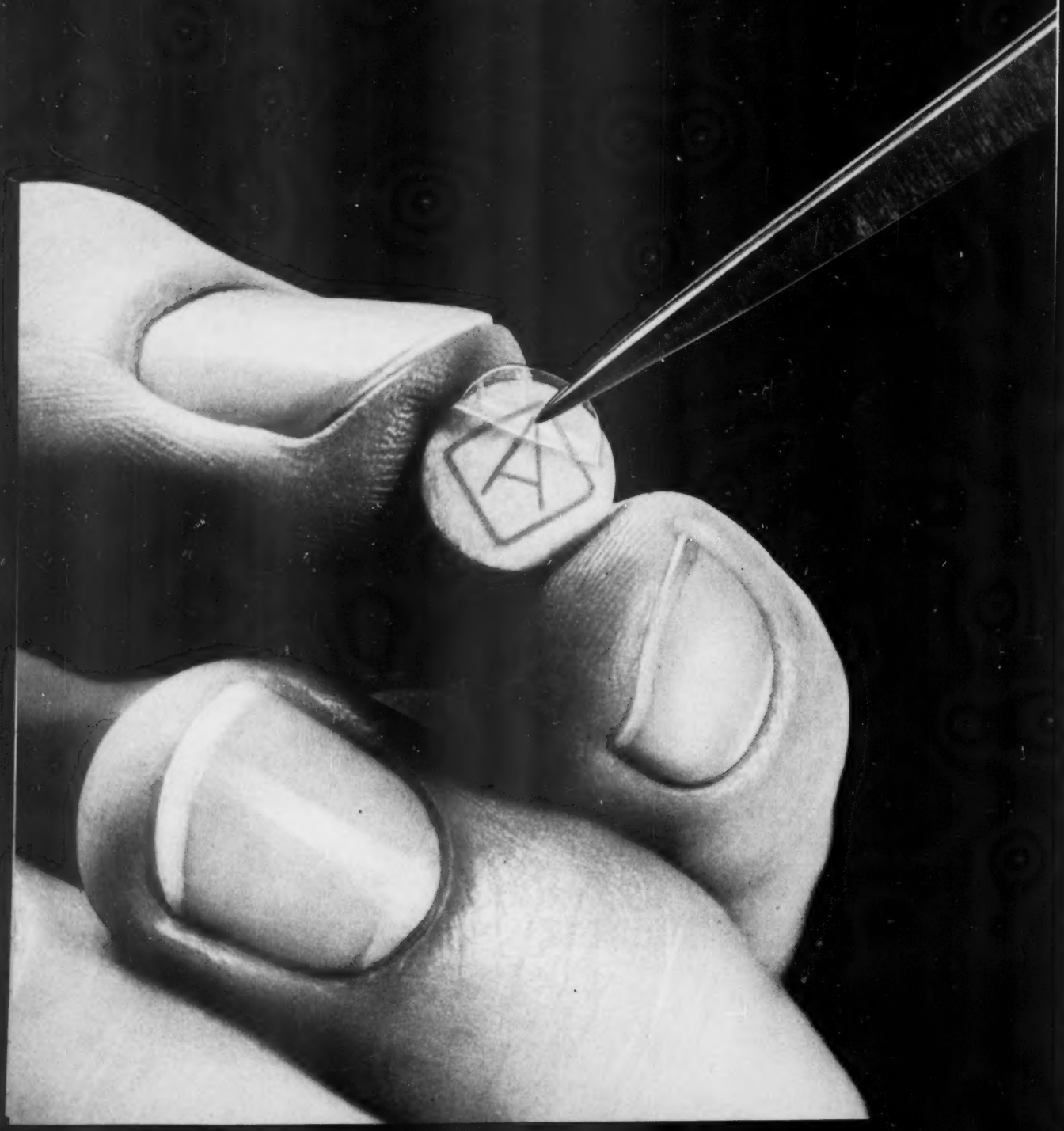

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Erythrocin® Stearate

(Erythromycin Stearate, Abbott)

disintegrates faster than enteric-coated erythromycin

TISSUE-THIN FILMTAB COATING (marketed only by Abbott) actually starts to dissolve within 30 seconds after administration —makes ERYTHROCIN available for immediate absorption. Tests show that new Stearate form definitely protects ERYTHROCIN from gastric juices.

BECAUSE THERE'S NO DELAY FROM AN ENTERIC COATING, your patient gets high, inhibitory blood levels within 2 hours—instead of 4-6 as before. Peak concentration at 4 hours, with significant levels for 8 hours.

USE FILMTAB ERYTHROCIN STEARATE against the cocci . . . and especially when the organism is resistant to other antibiotics. Low in toxicity—*it's less likely to alter normal intestinal flora than most oral antibiotics.* Conveniently sized (100, 200 mg.) in bottles of 25 and 100. Abbott

*TM for Abbott's film sealed tablets, pat. applied for

ON EVERY COUNT **Superior**

VITAMIN SUPPLEMENTS FOR INFANTS

Superior flavor Exceptionally pleasant "taste-tested" blend of flavors carefully protected during manufacture . . . no unpleasant aftertaste . . . readily accepted without coaxing.

Superior stability Outstanding stability is achieved by Mead's specially developed solution. Poly-Vi-Sol and Tri-Vi-Sol do not require refrigeration . . . no expiration dates on labels . . . they may be safely autoclaved with the formula.

Superior convenience Light, free-flowing . . . no mixing necessary . . . calibrated droppers assure easy, accurate dosage. For infants, drop directly into the mouth. For children, measure into a spoon.

Superior hypoallergenicity Poly-Vi-Sol® and Tri-Vi-Sol® supply crystalline vitamins in a completely hypoallergenic solution.

Poly-Vi-Sol

Six essential vitamins for drop dosage

Each 0.6 cc. supplies:

Vitamin A	5000 units
Vitamin D	1000 units
Ascorbic acid	50 mg.
Thiamine	1 mg.
Riboflavin	0.8 mg.
Niacinamide	6 mg.

Tri-Vi-Sol

Vitamins A, D and C for drop dosage

Each 0.6 cc. supplies:

Vitamin A	5000 units
Vitamin D	1000 units
Ascorbic acid	50 mg.

Available in 15 cc. and 50 cc. dropper bottles

MEAD JOHNSON & COMPANY • EVANSVILLE, INDIANA, U. S. A. MEAD